Essays on Drug Development and Marketing

by

Su Zhang

Department of Economics
Duke University

Date: ______________________
Approved:

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Yi (Daniel) Xu, Co-supervisor

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David R. Ridley, Co-supervisor

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Henry G. Grabowski

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Bryan Bollinger

Dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the Department of Economics
in the Graduate School of Duke University
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Abstract

The dissertation consists of three chapters relating to drug development and marketing strategies. Chapter 1 studies strategic direct-to-consumer and direct-to-physician advertising in the pharmaceutical industry. It is well known that pharmaceutical manufacturers invest heavily in advertising prescription medications, but little is known about synergies between different advertising types. Using 2007 to 2008 data from the anticholesterol market and the border strategy, I find that a 10% increase in direct-to-consumer advertising per capita is associated with 0.3%-0.4% more physician detailing visits or 1% more detailing time for a given product in a given market. By further constructing and estimating a demand model, I find that advertising to consumers results in more physician visits. In addition, conditioning on visiting a physician, advertising to consumers increases the number of requests for the advertised brand from patients with private insurance. Finally, after controlling for the patient request, direct-to-physician advertising increases the number of prescriptions written for the promoted product. Chapter 2 examines the strategic interaction between government agencies in funding support for medical research. Using data from 2007-2014 on medical research funding for infectious and parasitic diseases, we examine how governments and foundations in 41 countries respond to funding changes by the US government (which accounts for half of the funding for these diseases). We find that a 10 percent increase in US govern-

ment funding for a disease is associated with a 2 to 3 percent reduction in funding for that disease by another government in the following year. Chapter 3 investigates how pharmaceutical companies make R&D decisions for neglected diseases. Using firm level R&D data, we find that a company develops more treatments for neglected diseases if its headquarters is in a country with former colonies where the diseases create the largest burden. These essays provide insights into the marketing and drug development strategy of pharmaceutical companies and funding strategies of government funders for medical research.

To my beloved families.

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Symbols

I use Greek letters to represent variables in my theoretical and empirical models in my dissertation. I use subscripts to index specific observations and superscripts to index different behaviors. For example, δ^r_{mkt} may represent the mean request utility for product k in market m in time period t. With each new variable introduced in the body of my dissertation, I explain what it to refers to and how to interpret any subscripts and superscripts used.

Abbreviations

Below I list the set of abbreviations used in my dissertation as well as a brief corresponding description for each item.

AIDS	Acquired immunodeficiency syndrome , a fatal condition allows life-threatening opportunistic infections and cancers to thrive.
BN	Billion, the number equals to the thousands of million.
CEO	Chief executive officer, one of the most senior leader in charge of managing an organization.
CSR	Corporate social responsibility, a form of corporate self-regulation to assess and take responsibility to ensure its active compliance with social ethical standards.

DALYs	Disability-adjusted life years, a measure of disease burden.
DMA	Designated market area, a group of counties that form an exclusive geographic area in which the home market television stations hold a dominance of total hours viewed.
DTCA	Direct-to-consumer advertising, the marketing of pharmaceutical products and medical devices directed toward consumers instead of healthcare service providers.
DTP	Direct-to-physician advertising, the marketing of pharmaceutical products and medical devices directed toward healthcare service providers.
GDP	Gross domestic product, a monetary measure of the value of all final goods and services produced in a period of time within a whole country or a region.
GHW	Raleigh-Durham, one of the designated market area in North Carolina.
GSK	GlaxoSmithKline, a pharmaceutical company whose headquarter is in the UK.
HIV	The human immunodeficiency virus, a lentivirus induces life-threatening opportunistic infections and cancers.
IV	Instrumental variables, an econometric method used to estimate causal relationships when controlled experiments are not feasible.
MM	Million, the number equals to the thousands of thousand.
MSA	Metropolitan statistical area, a geographical region with a relatively high population density at its core and close economic ties throughout the area.
NGO	Non-governmental organizations, nonprofit organizations that are independent of governments and international governmental organizations.
NIH	US National Institutes of Health, a part of the US Department of Health and Human Services, the largest biomedical research agency in the world.

OLS	Ordinary least squares, an econometric method to estimate the unknown parameters in a linear regression model.
R&D	Research and development, the work towards new products or improvement of existing products.
RD	Television, a telecommunication tool used for transmitting moving images.
TV	Television, a telecommunication tool used for transmitting moving images.
WHO	The World Health Organization, an international governmental organization and a specialized agency of the United Nations focusing on international public health.

Acknowledgements

I would like to earnestly thank my committee co-chairs, Daniel Xu and David Ridley, for their valuable guidance, tremendous encouragement, and generous support throughout my PhD program. I am grateful to my committee members, Bryan Bollinger and Henry Grabowski. I benefited immensely from discussing my research works with each of them.

I am also thankful to all seminar and lunch group attendants at Duke University for their helpful suggestions. The second chapter is coauthored with David Ridley and Margaret Kyle and the third chapter is coauthored with David Ridley. I would like to thank them for all their insight and work on these two chapters.

1

Introduction

The dissertation consists of three chapters relating to drug development and marketing strategies. Chapter 1 studies strategic direct-to-consumer and direct-to-physician advertising in the pharmaceutical industry. Chapter 2 examines the strategic interaction between government agencies in funding support for medical research. Chapter 3 investigates how pharmaceutical companies make R&D decisions for neglected diseases.

The first chapter studies how pharmaceutical companies make marketing strategies.It is well known that pharmaceutical manufacturers invest heavily in advertising prescription medications, but little is known about synergies between different advertising types. Furthermore, little is known about whether patients and physicians respond differently to different types of advertising. Estimating a causal relationship is challenging because advertising is not randomly assigned. Because the segmentation of television and radio markets are discrete and exogenous, comparing advertising efforts and demand for prescription medications across borders may help identify causal effects between medication advertising and prescriptions for brand-name medications. Using 2007 to 2008 data from the anticholesterol market and the border strategy, I find that a 10% increase in direct-to-consumer advertising per capita is associated with 0.3%-0.4% more physician detailing visits or 1% more detailing time for a given product in a given market. By further constructing and estimating a demand model that separately models physicians' and patients' decisions, I find that advertising to consumers results in more physician visits. In addition, conditioning on visiting a physician, advertising to consumers increases the number of requests for the advertised brand from patients with private insurance. Finally, after controlling for the patient request, direct-to-physician advertising increases the number of prescriptions written for the promoted product.

How do governments respond to other governments when providing a global public good? Using data from 2007-2014 on medical research funding for infectious and parasitic diseases, we examine how governments and foundations in 41 countries respond to funding changes by the US government (which accounts for half of the funding for these diseases). Because funding across governments might be positively correlated due to unobserved drivers they have in common, we use variation in the representation of research-intensive universities on US Congressional appropriations committees as an instrument for US funding. We find that a 10 percent increase in US government funding for a disease is associated with a 2 to 3 percent reduction in funding for that disease by another government in the following year.

Companies increasingly engage in corporate social initiatives, but little is known about who cares and why. We measure corporate social initiatives as developing drugs for neglected diseases endemic in poor countries and charging low prices for all drugs (including heart disease and diabetes) for people in poor countries. These activities are costly, unlikely to be directly profitable, and can help millions of people. We find that companies most amenable to social initiatives are those with connections to the patients or the disease areas. We find that a company develops more treatments for neglected diseases if its headquarters is in a country with former colonies where the diseases create the largest burden. For example, Belgium, Britain, and France have former colonies in which diseases of poverty are prevalent, and companies based in Belgium, Britain, and France conduct more clinical trials for those diseases. Furthermore, companies based in countries with stronger colonial ties charge lower prices for all of their drugs in developing countries, including drugs for heart disease and diabetes. Finally, we show that these initiatives are unprofitable, unlike other forms of corporate social responsibility, such as environmental efforts, that can reduce costs and improve efficiency.

2

Did Relaxing Regulations on Medication TV Advertisements Cause More Advertising to Physicians?

2.1 Introduction

It is well known that pharmaceutical manufacturers invest heavily in advertising prescription medications, but little is known about synergies between different advertising types. Advertising to consumers and advertising to physicians could be complements or substitutes. Alternatively, these types of advertising might be unrelated; for example, pharmaceutical manufacturers might not be able to adjust advertising to physicians as fast as advertising to consumers because they cannot quickly hire new pharmaceutical sales representatives who have strong relationships with physicians.

I investigate synergies between direct-to-consumer advertising (DTCA) and direct-to-physician (DTP) advertising decisions. I also examine how advertising differentially affects demand for advertised products from patients and physicians. Physicians and patients jointly choose prescription medications, although they may make different choices (Stevenson et al., 2000). Patients visit their physicians to seek treatment for illness. Upon patient visit, the physician makes a diagnosis and may select medication treatment. Patients may be involved in the prescription decision by requesting a certain brand or type of medication. In the US, patients tend to be actively engaged in prescription decisions. A survey conducted by the Kaiser Family Foundation found that nearly one third of patients have requested a certain brand-name medication when talking to their physicians, and physicians fulfill half of these requests (Figure 2.1). By simultaneously promoting products to both patients and physicians, pharmaceutical companies might realize further financial gains than by focusing their promotional efforts on either party alone. Indeed, DTCA and DTP advertising are found to be complementary: The return-on-investment of DTP advertising has increased with DTCA expenditure and vice versa (Narayanan et al., 2004). However, we have little evidence to support strategic coordination of DTCA and DTP advertising. In addition, the evolution of the synergistic relationship between DTCA and DTP advertising is not well understood.

In this paper, I present the first empirical evidence of strategic DTCA and DTP advertising through a case study in the anticholesterol market. Given the identified coordination between DTCA and DTP advertising, I construct a demand model to explore how DTCA affects patients, how DTP advertising affects physicians, and how DTCA and DTP jointly affect the interactions between patients and physicians. Finally, I derive the necessary conditions for DTCA and DTP to be synergistic based on the constructed model and test these conditions by estimating the model.

Identifying a strategic coordination between DTCA and DTP advertising is not straightforward, and neither is identifying the impacts of marketing efforts on consumers. There could be some unobserved factors or events that affect DTCA, DTP advertising, and pharmaceutical product demand simultaneously. For example, an educational meeting or an academic conference in a given market for a given product might result in greater local DTP advertising, DTCA advertising, and demand for that product at the same time due to higher public awareness or goodwill. To solve this endogeneity problem, I explore the exogenous and discrete feature of the DTCA market and use the border strategy (Shapiro, 2017). Specifically, I compare DTCA and DTP efforts for a pharmaceutical product, the number of prescriptions written for that product, and the number of patient requests for that product across counties along the two sides of a DTCA market border.

I find that a 10% increase in DTCA expenditure per capita results in 0.3%-0.4% more detailing visits or 1% more detailing time for a given product in a given market. Based on the evidence, I establish a demand model that incorporates synergistic DTP and DTCA. Specifically, my model allows DTCA to affect patients by altering their physician visit and brand request decisions, and allows DTP advertising and patient brand request decisions to affect physicians by changing their prescription choices. By applying the border strategy on a novel data set, I estimate the model and identify the causal relationship between pharmaceutical marketing efforts and physician visit, brand request, and prescription choice, respectively. I find that DTCA efforts result in more physician visits. In addition, conditioning on a physician visit, DTCA increases the number of requests for the advertised brand from patients with private insurance. Finally, after controlling for patient request, DTP advertising increases the number of prescriptions written by physicians for the promoted product.

While most published economics and marketing analyses omit patients when modeling prescription decisions, previous medical research shows that patients' participation in the decision process is non-trivial (Gregory et al., 2011) and should be encouraged (Makoul et al., 1995; Britten et al., 2000). In addition, patients' requests have been found to be correlated with the number of prescriptions written (Prosser et al., 2003; Liu and Gupta, 2011; Stremersch et al., 2013; McKinlay et al., 2014) and services provided in other health care markets (Shih and Tai-seale, 2012). For example, physicians sometimes prescribe a brand-name product to a patient because a patient requests the brand even when a generic alternative is available (Division et al., 2013). Both market structure and payment models can affect the direction and magnitude of the correlations. For instance, more competition induces physicians to accommodate more patient requests when physicians are paid on a fee-for-service basis but less when physicians are in a managed care environment (Fang and Rizzo, 2009). However, most of these analyses either relied on descriptive case studies or did not causally identify the relationship between patients' product requests and physicians' prescription decisions. By constructing a structural model, this paper rationalizes the decisions made by patients and physicians separately and causally identifies how patients' requests affect physicians' prescription decisions.

Previous research has demonstrated that pharmaceutical marketing can positively impact pharmaceutical demand in both the internal and external margins. For example, DTCA has been found to be able to expand the market by inducing more patients to visit their physicians, (Iizuka and Jin, 2005) and the spillover effect is found across products within a medication class and also across different medication classes (Jayawardhana, 2013; Sinkinson and Starc, 2015; Shapiro, 2017). Unlike DTCA, which mainly affects pharmaceutical demand externally, DTP advertising primarily affects pharmaceutical demand internally. For instance, DTP advertising has a medication-specific positive effect on physician prescribing decisions; that is, DTP advertising increases demand for the advertised branded product (Ridley, 2015) and its generic alternatives (Ching and Ishihara, 2012). The magnitude of the DTP advertising impact is positively associated with scientific evidence (Azoulay, 2002; Venkataraman and Stremersch, 2007; Ching and Ishihara, 2010) and publicity (Ching et al., 2016). However, previous work does not separately identify how DTP advertising affects physicians and how DTCA affects patients because patients' decisions are seldom evaluated. Using the border strategy and fixed effects at the product-market-time level on a novel data set that includes detailed patients actions, I causally identify how patients and physicians are affected by DTCA and DTP advertising separately.

Compared with the impact of pharmaceutical advertising on product demand, factors that affect pharmaceutical advertising are less well explored. Earlier research shows that medications that are novel, of high quality, and indicated for under-treated diseases are more frequently included in DTCA efforts (Iizuka, 2004; de Frutos et al., 2013) and are associated with higher DTP advertising expenditures (de Frutos et al., 2013). In addition, pharmaceutical companies tend to advertise less for products whose patents are about to expire (Ellison and Ellison, 2011). My paper complements existing literature in this field by providing the first empirical evidence of strategic DTCA and DTP advertising that is, pharmaceutical companies adjust DTCA expenditure according to the DTP advertising efforts and vice versa. I also construct a demand model to explain the strategic interaction between DTP advertising and DTCA.

The remainder of this paper is organized as follows. Section 2 provides an overview of pharmaceutical advertising strategies and the anticholesterol medication market, and also describes the data sources used in this paper. Section 3 presents the identification strategy and the reduced form evidence of strategic DTCA and DTP advertising in the anticholesterol market. Section 4 proposes and estimates a demand model that explains the synergistic effect between DTCA and DTP advertising. Section 5 presents the empirical framework and estimates results of the demand model. Section 6 discusses the limitations of the analysis and its policy implications. Finally, Section 7 concludes the paper.

2.2 Background and Data

2.2.1 Pharmaceutical Advertising

There are two types of advertising campaigns in the prescription pharmaceutical market, DTP advertising and DTCA. Pharmaceutical companies use DTP advertising to inform about and persuade physicians to prescribe the advertised product by (1) hiring pharmaceutical sales representative to visit physicians (detailing) and distribute free samples, (2) printing advertisements in medical journals, and (3) organizing educational meetings for physicians. Detailing is the major form of DTP advertising. Detailing alone accounts for 36%- 48% of overall pharmaceutical DTP advertising expenditures (Gagnon and Lexchin, 2008). In the US, DTP advertising efforts are physician-specific and set based on past prescription volume (Manchanda and Chintagunta, 2004). According to an interview with a former pharmaceutical company CEO, companies typically make detailing decisions in advance of product launch because it takes time to hire and train sales representatives. However, contingent detailing strategies are made possible by hiring contractors and/or by altering the focus of product promotional efforts during a detailing visit.

On the contrary, DTCA is employed by pharmaceutical companies to inform and persuade consumers. The goal of DTCA is to help patients to learn about the benefits and potential risks of advertised medications and convince them to request the advertised brand from their physician. Pharmaceutical DTCA became widely implemented in the US in 1997. The most common format for pharmaceutical DTCA is television (TV) advertisements. Other formats include radio, print, and digital (online) advertisements. Pharmaceutical companies purchase advertising slots from advertising agencies in two ways: (1) through the upfront market and (2) through the spot market. In the upfront market, advertising spaces are determined annually, whereas in the spot market, pharmaceutical companies have more flexibility and can adjust advertising plans contingently. Companies can purchase either national DTCA, which may be seen by consumers all over the US, or local DTCA, which is broadcast to a specific market. The local DTCA market is segmented by designated market areas (DMAs). According to Kantar Media, a DMA is *a group of counties that form an exclusive geographic area in which the home market television stations hold a dominance of total hours viewed.* The concept of DMAs is also used by regulators in making policies[1].

Because generic medications are treated as therapeutically equivalent alternatives to their branded counterparts in the US, only branded products are advertised to physicians and/or patients. However, generic products compete with each other and their branded alternatives in dimensions other than marketing. For example, generic products are priced substantially lower than their branded counterparts.

Although pharmaceutical DTP advertising and DTCA can be both informative and

[1] FCC: Nielsen DMAs Still Best Definition of TV Markets. NewBay Media. June 13, 2016. http://www.broadcastingcable.com/news/washington/fcc-nielsen-dmas-still-best-definition-tv-markets/157246. Accessed October 20th, 2017.

persuasive (Berndt, 2005; Narayanan et al., 2005), I focus here on the persuasive role of DTP advertising and DTCA. As will be discussed in Section 3 (Reduced Form Evidence), my analysis focuses on the statin market between 2007 and 2008, 20 years after the initial launch of a medication in this class. As of 2007 to 2008, statins had become the most widely prescribed class of lipid-lowering medications and included several molecules with annual sales of more than $1 billion US dollars, including Lipitor (atorvastatin), the most widely prescribed statin medication. Therefore, it is reasonable to assume that the primary function of advertising in the anticholesterol market is persuasion instead of information.

2.2.2 Anticholesterol Market

Although the prevalence of abnormally high blood lipid levels, or hyperlipidemia, among the US population 40 years of age and older has dropped significantly from a high of 59% in the late 1970s, it is still among the most prevalent and serious health conditions in the US. The Centers for Disease Control and Prevention reported that in 2010, about 27% of US adults 40 years of age had hyperlipidemia, and more than 20% of US adults 40 years of age were taking cholesterol-lowering medications (Kuklina et al., 2013).

Statins are the most widely used class of anticholesterol medications since their introduction in the late 1980s. During the sample period, there were eleven molecules in the statin class, including seven different statins and four different statin combination therapies, on the market. Four of these eleven products were under patent protection and advertised by their sponsor companies. Other than the statins, there were two additional anticholesterol medications (Tricor [fenofibrate] and Zetia [ezetimibe]) that were advertised by their sponsors during the sample period (Table 2.5).

The overall structure of the anticholesterol market was stable between 2007 and 2008. Only one major new brand, Simcor (niacin/simvastatin), entered the market in March 2008. The six branded products under patent protection accounted for more than 60% of the overall prescriptions for anticholesterol medications during the 24-month period (Figure 2.3), while the aggregate share of unit sales decreased from more than 60% at the beginning of 2007 to about 55% at the end of 2008 (Figure 2.3). This decreasing trend in aggregate share of unit sales was caused by the entry of the generic version of Zocor (simvastatin), whose patent expired in 2006.

Across the sample period, Lipitor, Crestor (rosuvastatin calcium), and Vytorin (ezetimibe and simvastatin) were the branded statin/statin combination products with the greatest DTP advertising efforts as measured by both the number of detailing visits and weighted detailing minutes (Figure 2.5 and Figure 2.6). On average, Lipitor, Crestor, and Vytorin sales representatives visited physicians more than 8000 times and spent more than 50,000 minutes on each product per month. Similar patterns were observed for DTCA efforts (Figure 2.7). However, the differences in expenditures across products were smaller while the variation within products but across time was larger for DTCA than for DTP advertising efforts. The only branded new entrant in the sample period, Simcor, made substantial detailing efforts but spent almost nothing on DTCA[2].

2.2.3 Data

Data used in this paper come from three different sources. Physician-level demand and detailing data were obtained from BrandImpactRx. Market level DTCA data were provided by Ad$pender from Kantar Media. County level demographic data were collected

[2] It is a common marketing strategy employed by new entrants in the pharmaceutical industry because companies prefer to promote their products to physicians before patients.

from the US Census Bureau.

DTP Advertising and Prescriptions

BrandImpactRx provided physician-level monthly detailing and prescription data from January 2007 to December 2008. The data vendor, AlphaImpactRx, an IMS subsidiary, collected data from a representative sample of individual physicians, balanced across geographic locations, specialties, and prescription volumes. Specifically, for a given physician, the detailing data recorded the number of detailing visits and the time spent on each product during each visit for all anticholesterol medications. The prescription data included all medication prescriptions written by that physician in a given month. For each individual prescription, the prescription data included the name of the prescribed brand, the type of health insurance the patient had, whether or not the patient had requested any branded product, and the name of the requested brand. The data were longitudinal. Multiple-period observations were available for each physician. Physician location information, represented by a 5-digit zip code, was obtained from a separate file provided by BrandImpactRx . I measured DTP advertising efforts per product in two ways: (1) the total number of detailing visits and (2) the total time spent detailing a given product per physician per month.

Because BrandImpactRx does not record prescription information for patients who visit a physician but do not receive a prescription, I used the total number of prescriptions to approximate the number of patient visits for a given physician.

DTCA

Ad$pender provided monthly DTCA units and expenditure data at the prescription product level for all anticholesterol medications in the top 101 DMAs in the US. Because advertisements broadcast at different times had a different audience size and were priced at different levels, in this analysis I used DTCA expenditures rather than units to measure DTCA efforts. Following Shapiro (2017), I rescaled DTCA expenditures by population in the local market, which allowed me to measure national and local advertising volume comparably. Specifically, I defined the market level DTCA efforts as the sum of the national advertising expenditures divided by the national population and the market level advertising expenditures divided by the market population.

Demographic Information

I collected zip codes, population information, and the number of physicians by county from the Current Population Survey provided by the US Census Bureau.

The data were merged using the following steps: I first assigned each physician to a given county by the 5-digit zip code. Then I aggregated DTP advertising efforts per product per month across counties in a given DMA-border indicator. Finally, I merged aggregated DTP advertising data and DTCA data by product, date, and DMA-border indicator.

2.3 Reduced Form Evidence

In this section, I present the reduced-form evidence of strategic advertising by showing that in a given market, a pharmaceutical company tends to invest more in both DTCA and DTP advertising simultaneously, and I discuss the identification strategy.

I model the DTP advertising efforts from brand k in market m at time t as a linear function of its own DTCA efforts:

$$\mathrm{DTP}_{kmt} = \gamma_0^m + \gamma_1^m \mathrm{DTCA}_{kmt} + \gamma_2^m X_{kt} + \gamma_3^m X_{mt} + \epsilon_{kmt},$$

where X_{kt} and X_{mt} are a set of brand-time and market-time control variables.

2.3.1 Identification

Because both DTP advertising and DTCA are not randomly determined, one potential challenge for identification is endogeneity. Following Shapiro (2017), I use the border strategy to address the endogeneity concern. The border strategy relies on the exogenous and discrete nature of the DMA border. The border of each DMA is defined by AC Nielsen based on the local TV and radio programs that the residents can watch and are most interested in within a given county. As a result, households living on different sides of the DMA border tend to be exposed to different local advertising content. In addition, the location of the border is orthogonal to the factors that affect DTCA decisions of pharmaceutical companies.

To illustrate how border strategy works, consider Greensboro-High Point-Winston Salem (GHW) and Raleigh-Durham (RD), two adjacent DMAs in North Carolina as an example (Figure 2.11). Every county in the left (right) DMA, the GHW (RD), gets the same amount of the same advertising as every other county in the same DMA. Meanwhile, every county in the GHW DMA might get different advertising and/or different amount of advertising from every county in the RD DMA. There are four counties in the GHW DMA that share a border with at least one county in the RD DMA, and there are four counties in the RD DMA share at least one border with a county in the GHW DMA. The border strategy will be to take those eight counties along the border as an experiment with two treatment groups (GHW and RD) in a given time period.

The Ad$pender data contains DTCA expenditure from anticholesterol products in the top 101 DMAs in the US (Figure 2.9). Merging DTCA expenditure data with detailing data leaves 93 DMAs with 186 borders (Figure 2.10). Both the detailing and the DTCA expenditure data are aggregated at the product-border-DMA-month level. Each border is treated as a separate experiment, where the adjacent counties across the DMA border serve as controls for each other.

To examine how drug companies make strategic DTCA and DTP advertising decisions, I use a modified difference-in-differences method specified as below:

$$\mathrm{DTP}_{kmbt} = \gamma_0^m + \gamma_1^m \mathrm{DTCA}_{kmbt} + \alpha_{kmb} + \alpha_{kbq} + \epsilon_{kmbt}, \tag{2.1}$$

where subscription b refers to border, α_{kmb} is a brand-market-border fixed effect and α_{kbq} is a brand-border-quarter fixed effect. The underlying identification assumption is that any differential trends in DTP advertising efforts between the two sides of the DMA border stem from differences in DTCA efforts, after controlling for the two sets of fixed effects.

This is a valid assumption because all the counties are bordering. Physicians and residents located in these counties tend to have similar characteristics. Determinants of DTP advertising efforts, other than the DTCA efforts, are likely to be comparable across counties along the DMA border. Therefore, by comparing DTCA and DTP advertising efforts in counties across a DMA border, I can determine if and how DTCA and DTP advertising are causally related.

2.3.2 Regression Results

The results show that for a given pharmaceutical company in a given market, an increase in DTCA expenditure resulted in more DTP advertising efforts when the latter are measured by total number of detailing visits and weighted minutes of detailing per product, and when level marketing efforts (Table 2.1) and log marketing efforts (Table 2.2) are included in the regression in the same period. Specifically, the log regression results show that a 10% increase in DTCA expenditure results in a 0.4% increase in the number of detailing visits and a 0.6% increase in weighted detailing minutes. The estimated effects from DTCA efforts on DTP advertising efforts is small but statistically significant. The small magnitude of effects can be explained by the fact that, comparing to the widely available DTCA broadcast slots, physicians' availability is quite limited. Therefore, the realized increase in DTP advertising efforts is unlikely to be of the same magnitude as that of DTCA efforts.

To explore other potential strategic interactions between DTCA and DTP advertising within and across products, I further include contemporaneous and lagged DTCA and DTP advertising efforts from competitors and lagged DTCA and DTP advertising for their own products in the same market (Table 2.3). Despite the remaining positive and significant correlation between concurrent detailing and DTCA for their own products, there is one additional notable finding; that is, increasing DTCA expenditure and DTP advertising from competitors causes pharmaceutical companies to increase their own DTP advertising efforts. While the former positive response of detailing with respect to competitors DTCA efforts might be induced by spillover effects of DTCA, the latter could be a case of prisoner's dilemma.

2.4 Demand Model

In this section I propose a demand model to show how DTCA and DTP advertising become synergistic. In this model, a patient makes two decisions: (1) whether or not to visit a physician and (2) whether or not to request a brand-name product. DTCA affects both of these decisions. Depending on a patient's visit and medication request, a physician decides which medication should be prescribed for that patient. DTP adverting affects a physician's prescription decision by increasing physician's goodwill with respect to the advertised brand.

I first describe how physicians make prescription choices, conditioning on patients' requests and DTP advertising. Then I show how patients make physician visit and prescription request decisions accounting for DTCA of branded products.

2.4.1 Physicians: Accommodation and Prescription Choices

Existing medical literature shows that physicians accommodate patients' requests partly because accommodation affects the patient satisfaction rate (Zgierska et al., 2012). A low patient satisfaction rate might lead to lower physician compensation (Frantsve and Kerns, 2007) or even voluntary disenrollment from the service provider (Safran et al., 2001), regardless of ex-post health condition improvement. Motivated by these findings, I allow physicians to accommodate both their own and patients' utilities when making prescription choice decisions.

A physician makes a prescription decision in two steps. First, a physician determines her accommodation pattern with respect to a patient's request, which is measured by parameter θ_p, to maximize her objective function, $f(\lambda(\theta_p), \Phi(\theta_p))$. λ stands for the expected patient inflow and Φ stands for the patient experience utility loss due to physician accommodation. Second, given the accommodation pattern, the physician chooses the brand that maximizes her own decision utility. I assume that the physician prefers to treat more patients, therefore $f_1 > 0$. In addition, I assume that the physician suffers from prescribing suboptimal[3] brands due to brand request accommodation, which implies that $f_2 < 0$. In the following sub-sections, I first define the decision utility function of the physician and show how physicians make brand choice decisions, taking the value of θ_p as a given. Then, I introduce $\lambda(\theta_p)$ and $\Phi(\theta_p)$ and discuss how the value of θ_p is determined.

Prescription Choices

I assume a physician makes a prescription choice based on the following decision utility function:

$$u_{pikt} = v_{pikt} + \theta_p A^c_{ikt}, \tag{2.2}$$

where A^c_{ikt} is a dummy indicating patient request and v_{pikt} refers to the experience utility patient i obtained from brand k at time t, from the perspective of the physician p. $A^c_{ikt} = 1$ if patient i requests brand k at time t. Otherwise it equals 0. θ_p measures the weight that the physician puts on the patient request when making prescription choices. A larger value of θ_p implies a larger impact from the patient request on a physician's brand choice decision. The weight of a patient's experience utility is normalized to 1.

v^p_{ikt} is a linear function of the physicians goodwill with respect to brand k, G^p_{kt}, plus a brand-time fixed effect, α_{kt}, capturing time-varying product level features, a physician-

[3] I assume patients lack the necessary knowledge to choose the optimal brand for their own conditions. Therefore, patient requests are always worse than, or equivalent to, the choice made by physicians alone.

brand fixed effect, $\alpha_p k$, capturing the physicians preference toward a certain brand k, a physician-time fixed effect, α_{pt}, capturing the physician's overall prescribing habit over time, and an i.i.d, logit information shock on the physician, ϵ^p_{ikt}:

$$\upsilon_{pikt} = \gamma^p_0 + \gamma^p_1 G_{pkt} + \alpha^p_{kt} + \alpha^p_{pk} + \alpha^p_{pt} + \epsilon_{pikt} = \delta^p_{pkt} + \epsilon_{pikt}. \tag{2.3}$$

I use δ^p_{pkt} to represent the mean utility of brand k at time t. Following previous published studies of pharmaceutical marketing, I assume G^p_{kt} is a log function of DTP advertising efforts of brand k at time t:

$$G_{pkt} = \log(1 + \mathrm{DTP}_{pkt}).$$

The probabilities of prescribing brand k depend on patients' requests. Normalizing the utility of the outside option to be 0[4], we have:

$$\begin{aligned}
\mathrm{Prob}(k|A^c_{ikt} = 1) &= \frac{\exp(\delta^p_{pkt} + \theta_p)}{1 + \exp(\delta^p_{pkt} + \theta_p) + \sum\limits_{j \neq k} \exp(\delta^p_{pjt})}, \\
\mathrm{Prob}(k|A^c_{ik't} = 1) &= \frac{\exp(\delta^p_{pkt})}{1 + \exp(\delta^p_{pk't} + \theta_p) + \sum\limits_{j \neq k'} \exp(\delta^p_{pjt})}, \qquad (2.4) \\
\mathrm{Prob}(k|A^c_{i0t} = 1) &= \frac{\exp(\delta^p_{pkt})}{1 + \sum\limits_{j} \exp(\delta^p_{pjt})}.
\end{aligned}$$

Given these conditional probabilities, the expected unconditional probability of fulfilling a patient request, $\mathrm{P}(Y)$, is equal to:

[4] The outside option includes branded statins whose patent expired before 2007 and their generic alternatives, plus anticholesterol medications in other classes I observed in the data.

$$\mathrm{P(Y)} = \sum_j \mathrm{Prob}(j|A^c_{ijt} = 1)\mathrm{Prob}(A^c_{ijt} = 1), \tag{2.5}$$

where $\mathrm{Prob}(A^c_{ijt} = 1)$ refers the probability that brand j is requested by the patient, which is formally defined by equation 2.9. To simplify the notation, I use $p_{k|k}$ to represent $\mathrm{Prob}(k|A^c_{ikt} = 1)$ and p^r_k to represent $\mathrm{Prob}(A^c_{ijt} = 1)$ for the remainder of the paper.

Accommodation Pattern

Now I show how θ_p is determined by the physician. Patients are assumed to be myopic in this model. As a result, the inflow of patients per physician, λ, depends on how accommodating the physician is, which is measured by the unconditional probability that a patient request would be fulfilled, P(Y): $\lambda = \lambda(\mathrm{P(Y)}) = \lambda(\theta_p)$. The more accommodating the physician is, the more patients would visit the physician. Therefore, $\lambda_{\theta_p} > 0$

The utility loss of patients due to physician accommodation, Φ, is determined by the absolute difference between the expected experience utility of patients when $\theta_p = 0$ and when $\theta_p > 0$:

$$\Phi = |\sum_j p^0_j v^p_{jt} - \sum_j p_j v^p_{jt}| = \Phi(\theta_p),$$

where p_k refers to the probability of brand k being prescribed and $p_k = \sum_j p_{k|j} p^r_j$, and $p^0_k = p_k(\theta_p = 0)$. Patients would suffer more in experience utility loss as the physician becomes more accommodating. Therefore, $\Phi_{\theta_p} < 0$.

Given the assumptions above, the physician determines the value of θ_p to solve the following optimization problem:

$$\begin{aligned}&\arg\max_{\theta_p} f(\lambda(\theta_p), \Phi(\theta_p))\\&s.t.: \lambda_{\theta_p} > 0, \Phi_{\theta_p} < 0.\end{aligned} \tag{2.6}$$

For the purpose of this paper, I do not explicitly define the function f and solve for the value of θ_p analytically. However, I display the trade-off between physician accommodation and patient experience utility maximization by simple numerical simulation in section 2.4.3.

2.4.2 Patients: Brand Request and Physician Visit

In this model, I assume patients make the following two decisions sequentially. First, they decide whether to visit their physicians or not. Then, conditioning on visit, they decide if and which brand to request. I solve the patients' problem in reverse: first, I discuss how patients make brand request decisions conditioning on visit. Then, I discuss how patients make physician visit decisions.

Brand Request

Given that the patient i visits a physician at time t, similar to equation 2.3, I assume the utility of taking brand k, according to the patient, u^c_{ikt}, depends on a patients goodwill with respect to that brand, G^c_{ikt}, a brand-time fixed effect, a market-brand fixed effect, and a logit demand shock:

$$u^c_{imkt} = \gamma^c_0 + \gamma^c_1 G^c_{imkt} + \alpha^c_{kt} + \alpha^c_{mk} + \epsilon^c_{imkt} = \delta^c_{imkt} + \epsilon^c_{imkt}, \tag{2.7}$$

the brand-time fixed effect captures time-varying product level features observed by the patient. The market-brand fixed effect captures time invariant, market-specific brand features. Similar to the physicians goodwill toward a brand, I assume G^c_{imkt} is a log function of DTCA of that brand aired in the market m where patient i is. Thus,

$$G^c_{imkt} = \log(1 + \mathrm{DTCA}_{mkt}). \tag{2.8}$$

Let $A^c_{ikt} = 1$ if patient i requests brand k during her visit at time t and $A^c_{ikt} = 0$ otherwise. The probability that brand k being requested, $p^r_i k$, is equal to:

$$p^r_{ik} = \frac{\exp(\delta^c_{imkt})}{1 + \sum\limits_j \exp(\delta^c_{imjt})} \tag{2.9}$$

Physician Visit

To simplify the analysis, this model assumes each patient can visit only one physician in a given period and the patient cannot choose which physician to visit. Patient i's utility of visiting her physician at time t, u^v_{imt}, is a linear function of the expected utility of existing medical treatment, G^v_{imt}, a time fixed effect, α^v_t, a physician fixed effect, α^v_p, and an i.i.d logit shock, ϵ^v_{imt}:

$$u^v_{imt} = \gamma^v_0 + \gamma^v_1 G^v_i mt + \alpha^v_t + \alpha^v_m + \epsilon^v_{imt} = \delta^v_{imt} + \epsilon^v_{imt}. \tag{2.10}$$

There are two components in G^v_{imt}. The first component is the expected utility from the advertised brands that the patient would request, and the second component is the expected utility of treatment that the patient would receive if her brand request is rejected. Formally:

$$G^v_{imt} = \mathrm{P(Y)}log[1 + \sum_j exp(\delta^r_{imjt})] + (1 - \mathrm{P(Y)})G_m, \tag{2.11}$$

where P(Y) refers to the probability of a patient request being fulfilled by the physician, which is defined in equation 2.5. G_m is a market-specific term representing the value of treatment received by the patient if her request is rejected. G_m cannot be unobserved by economists and cannot be separately identified from market fixed effects. In addition, I assume $G_m \leqslant log[\sum_j exp(\delta^r_{imjt})]$, which implies that from the patient's perspective, the inside options are always non-inferior than the backup treatment option.

Therefore, the probability that a patient would visit her physician is given by following equation:

$$p^v_{imt} = \frac{\exp(\delta^v_{imt})}{1 + \sum_j \exp(\delta^v_{imt})} \tag{2.12}$$

2.4.3 Numerical Simulation

Simulated correlations between θ_p and brand request fulfill rate $P(Y)$, between brand request fulfill rate and the probability of patient visit p^v, and between θ_p and patient utility loss Φ are consistent with the model prediction. The plots suggest that as the physician becomes more accommodating, she is more likely to fulfill her patients' requests (Figure 2.12a), and more patients would visit her (Figure 2.12b), but patients would suffer more in experience utility loss (Figure 2.12c).

2.4.4 Derivatives

In this sub-section, I describe the strategic implication of DTP advertising and DTCA generated by the demand model through deriving first order derivatives. Equation 2.12 defines the share of patients who visit physician p as the probability that a representative patient chooses to visit, p^v_{imt}. Likewise, equation 2.4 defines the market share of brand k for physician p conditioning on patient request for brand k' as the conditional probability of physician p prescribing brand k for each patient. Finally, equation 2.9 defines the share of patients who request brand k', which is equivalent to the probability of a representative patient who requests that brand. As a result, the market share of product k in market m at time t is:

$$\begin{aligned}
s_{kmt} = \sum_{p \in m} \frac{\exp(\delta^v_{mt})}{1+\exp(\delta^v_{mt})} [& \frac{\exp(\delta^c_{kt})}{1+\sum_j \exp(\delta^c_{jt})} \frac{\exp(\delta^p_{pkt}+\theta_p)}{1+\exp(\delta^p_{pkt}+\theta_p)+\sum_{j\neq k}\exp(\delta^p_{jt})} + \\
& \sum_{k'\neq k,0} \frac{\exp(\delta^c_{k't})}{1+\sum_j \exp(\delta^c_{jt})} \frac{\exp(\delta^p_{pkt})}{1+\exp(\delta^p_{pk't}+\theta_p)+\sum_{j\neq k'}\exp(\delta^p_{jt})} + \\
& \frac{1}{1+\sum_j \exp(\delta^c_{jt})} \frac{\exp(\delta^p_{pkt})}{1+\sum_j \exp(\delta^p_{jt})}]
\end{aligned} \tag{2.13}$$

Subscription i is omitted as patients within a given market are homogeneous after controlling for the DTCA expenditure and a set of fixed effects.

Given the share defined above, the derivative of s_{kmt} with respect to DTP advertising toward physician p at time t is:

$$\frac{\partial s_{kmt}}{\partial DTP_{kpt}} = \gamma_p s^v_{mt} \sum_{k'} s^r_{k'|mvt} s^p_{k|k'} (1 - s^p_{k|k'}) \frac{1}{DTP_{pkt}} > 0 \text{ if } \gamma_p > 0. \tag{2.14}$$

Equation (2.14) shows that DTP advertising benefits pharmaceutical companies by increasing the share of the advertised brand being prescribed, whether the brand is requested by patients or not.

The derivative of s_{kmt} with respect to DTCA toward patients in market m at time t is:

$$\begin{aligned} \frac{\partial s_{kmt}}{\partial DTCA_{mkt}} = \sum_{p \in m} [& s^v_{mt}(1 - s^v_{mt}) \underbrace{\frac{\partial \delta^v_{mt}}{\partial DTCA_{mkt}}}_{>0} \sum_{k'} s^r_{k'|mvt} s^p_{k|k'} \\ & + s^v_{mt} \gamma_r s^r_{k|mvt} \sum_{k' \neq k} s^r_{k'|mvt} \underbrace{(s^p_{k|k} - s^p_{k|k'})}_{>0 \text{ if } \theta_p > 0} \frac{1}{DTCA_{mkt}}], \end{aligned} \tag{2.15}$$

pharmaceutical companies benefit from DTCA because the latter encourages patients to talk to their physicians (market expansion), which is captured by the first term in equation (2.15), and to request the advertised brands (business stealing), which is captured by the second term in equation (2.15).

Similarly, the first order derivative of s_{kmt} with respect to competitor's DTP advertising and DTCA is:

$$\frac{\partial s_{kmt}}{\partial \text{DTP}_{pjt}} = -\gamma_p s^v_{mt} \sum_{k'} s^r_{k'|mvt} s^p_{k|k'} s^p_{j|k'} \frac{1}{DTP_{pjt}} < 0,$$

$$\frac{\partial s_{kmt}}{\partial \text{DTC}_{mjt}} = \sum_{p \in m} [\underbrace{\frac{\partial s^v_{mt}}{\partial DTC_{mjt}} \sum_{k'} s^r_{k'|mvt} s^p_{k|k'}}_{>0,\text{market expansion}} + s^v_{pt} \sum_{k'} \frac{\partial s^r_{k'|mvt}}{\partial DTC_{mjt}} s^p_{k|k'}]. \tag{2.16}$$

Competitor's DTP advertising reduces a firm's own market share because the former persuades physicians to prescribe a competitor's product regardless of patients' requests. The impacts of competitor's DTCA on a firms own market share are not obvious. On the one hand, the competitor's DTCA would encourage patients to request the competitor's product. On the other hand, the competitors DTCA encourages more physician visits by patients. While the former impact is negative, the latter impact is positive. The overall effect of a rival's DTCA depends on which effect dominates.

The cross derivative of s_{kmt} with respect to a firms own DTP advertising and DTCA is:

$$\begin{aligned} \frac{\partial s_{kmt}}{\partial DTP_{pkt} \partial DTCA_{mkt}} = & \underbrace{\gamma_p \frac{\partial s^v_{mt}}{\partial DTCA_{mkt}} \sum_{k'} s^r_{k'|mvt} s^p_{k|k'} (1 - s^p_{k|k'}) \frac{1}{DTP_{pkt}}}_{>0,\text{ market expansion}} + \\ & \gamma_p s^v_{mt} \sum_{k'} \frac{\partial s^r_{k'|mvt}}{\partial DTCA_{mkt}} s^p_{k|k'} (1 - s^p_{k|k'}) \frac{1}{DTP_{pkt}}. \end{aligned} \tag{2.17}$$

the first term on the right-hand-side of equation (2.18) shows that increasing DTCA efforts might improve the marginal return of DTP advertising by attracting more patients to visit their physicians. Meanwhile, according to equation (2.15) and (2.16), the sign on the second term, which captures the business stealing effects of DTCA, can be either positive or negative. The intuition is that DTP advertising would encourage physicians to prescribe the brand being detailed regardless of patients' requests, while DTCA would increase the share of patients who request the advertised brand but decrease the share of patients who request other brands.

Further expanding equation (2.18), we can show that:

$$\frac{\partial s_{kmt}}{\partial DTP_{pkt} \partial DTCA_{mkt}} \leqslant 0 \text{ if } \gamma^r \leqslant 0 \mid \gamma^p \leqslant 0. \tag{2.18}$$

In other words, the necessary conditions of synergistic DTCA and DTP advertising are $\gamma^r > 0$ and $\gamma^p > 0$. In addition, the synergistic effect is non-decreasing in γ^v and θ^p[5]. Therefore, the four following hypotheses will be tested in Section 5, Empirical Methodology and Demand Estimation:

Hypothesis 1. *DTCA encourages patients to request the advertised brand, or formally,* $\gamma^r > 0$.

Hypothesis 2. *DTP advertising encourages physicians to prescribe the detailed brand, regardless of patients' requests, or formally,* $\gamma^p > 0$.

Hypothesis 3. *DTCA encourages patients to visit physicians, or formally,* $\gamma^v > 0$.

Hypothesis 4. *Physicians value patients' requests, or formally,* $\theta^p > 0$.

2.5 Empirical Methodology and Demand Estimation

In this section, I present the empirical framework and estimation results for the demand model. First, I describe the identification strategy. Then, I present and discuss the

[5] Please refer to the Appendix for more details.

demand estimation results. Finally, I display the synergistic effects between DTCA and DTP advertising through simulating a single-agent profit maximization problem.

2.5.1 Identification

DTP Advertising and Physician's Prescribing Decision

As stated in the theory section, the probability of physician p prescribing brand k at time t depends on a patient's request, a manufacturers DTP advertising efforts, and brand characteristics.

The identification of how DTP advertising affects physician prescribing stems from the variation of brand shares when patients choose to request the outside option. Specifically, given that patients request the outside option, the share of brand k and the outside option at time t is:

$$s^p_{k|0,t} = \frac{exp(\delta^p_{pkt})}{1 + \sum\limits_{k'} exp(\delta^p_{pk't})} \tag{2.19}$$

and

$$s^p_{0|0,t} = \frac{1}{1 + \sum\limits_{k'} exp(\delta^p_{pk't})}, \tag{2.20}$$

where δ^p_{pkt} is defined in equation 2.3. Take a log of both sides of equation 2.19 and 2.20 and compute the difference:

$$\ln s^p_{k|0,t} - lns^p_{0|0,t} = \delta^p_{pkt} = \gamma^p_0 + \gamma^p_1 \ln \mathrm{DTP}_{pkt} + \alpha^p_{kt} + \alpha^p_{pk} + \alpha^p_{pt}.$$

One remaining concern with respect to equation 2.21 is that there might be some physician-brand-month specific unobserved factors that could affect both a physician's prescription decisions and a firm's DTP advertising decisions simultaneously. Ideally, the instrumental variable method can address this endogeneity problem. However, the instrumental variable method is unlikely to find an exogenous shock at the physician-brand-month level. To partially address this issue, I include an area-brand-time fixed effect, α^p_{apt}, in the regression. I define the area in two ways: (1) metropolitan statistical area (MSA), and (2) 5-digit zip code area. Therefore, the regression equation becomes:

$$\ln s^p_{k|0,t} - lns^p_{0|0,t} = \delta^p_{pkt} = \gamma^p_0 + \gamma^p_1 \ln \mathrm{DTP}_{pkt} + \alpha^p_{akt} + \alpha^p_{pk} + \alpha^p_{pt}. \tag{2.21}$$

Parameter γ^p_1 in equation 2.21 measures how DTP advertising affects a physician's prescribing decisions.

Patient Request and Physician's Prescribing Decision

The share of brand k being prescribed by the physician conditioning on patient request is:

$$s^p_{k|k,t} = \frac{exp(\delta^p_{pkt} + \theta_p)}{1 + \sum\limits_{k' \neq k} exp(\delta^p_{pk't}) + exp(\delta^p_{pkt} + \theta_p)} \tag{2.22}$$

Accordingly, the share of outside option when brand k is requested is equal to:

$$s^p_{0|k,t} = \frac{1}{1 + \sum\limits_{k' \neq k} exp(\delta^p_{pk't}) + exp(\delta^p_{pkt} + \theta_p)}, \tag{2.23}$$

where δ^p_{pkt} is defined in equation 2.3. Subtracting the log of equation 2.23 from the log of equation 2.22 gives us:

$$\ln s^p_{k|k,t} - lns^p_{0|k,t} = \gamma^p_0 + \gamma^p_1 \ln \mathrm{DTP}^p_{kt} + \gamma^p_2 A^c kt + \alpha^p_{kt} + \alpha^p_{pk} + \alpha^p_{pt}. \tag{2.24}$$

Further subtract equation (2.21) from equation (2.24):

$$(\ln s^p_{k|k,t} - lns^p_{0|k,t}) - (\ln s^p_{k|0,t} - lns^p_{0|0,t}) = \theta_p A^c_{kt}. \tag{2.25}$$

Granted that the model is correctly specified, an ordinary least squares regression of equation (2.25) provides an unbiased estimate of θ_p, the impact of patient request on physician prescribing choice.

DTCA and Patient's Request Decision

The share of patients who would request brand k is:

$$s^r_{mkt} = \frac{\exp(\delta^c_{mkt})}{1 + \sum\limits_j \exp(\delta^c_{mjt})}, \tag{2.26}$$

and the share of patients who would request an outside option is:

$$s^r_{0t} = \frac{1}{1 + \sum\limits_j \exp(\delta^c_{mjt})}, \tag{2.27}$$

where δ^c_{kt} is defined by equation 2.7. After taking the log of both sides of the equations and subtracting equation 2.27 from equation 2.26 we have:

$$\ln s^r_{mkt} - \ln s^r_{m0t} = \gamma^c_0 + \gamma^c_1 \ln \mathrm{DTCA}_{mkt} + \alpha^c_{kt} + \alpha^c_{mk}.$$

Because both DTCA and patient request are not randomly determined, identifying γ_1^c is not straightforward. For example, there might be some unobserved brand-market-time specific factors that affect both patient request and a pharmaceutical firms DTCA decisions. Like equation 2.1, I use border strategy to address the endogeneity concern of DTCA efforts. Specifically, I compare the brand request and brand-specific DTCA efforts across counties along the DMA border after controlling for the brand-border-DMA fixed effect and the brand-border-quarter fixed effect:

$$\ln s_{mkt}^r - \ln s_{m0t}^r = \gamma_0^c + \gamma_1^c \ln \mathrm{DTCA}_{kmt} + \alpha_{kbm}^c + \alpha_{kbq}^c. \tag{2.28}$$

DTCA and Patient's Visit Decision

The share of patients in each market who choose to visit a physician is summarized by:

$$\ln s_{mt}^v = \frac{\exp(\delta_{mt}^v)}{1 + exp(\delta_{mt}^v)}, \tag{2.29}$$

where δ_{pvt} is defined by equation 2.10. If we normalize the utility of not visiting to be 0, take the log of both sides of the equation, and compute the difference, we have:

$$\ln s_{mt}^v - \ln(1 - s_{mt}^v) = \gamma_0^v + \gamma_1^v G^v + \alpha_m^v + \alpha_t^v, \tag{2.30}$$

Substituting in equation 2.11 and rearranging the equation we have:

$$\ln s_{mt}^v - \ln(1 - s_{mt}^v) = \gamma_0^v + \bar{\gamma}_1^v \ln[\sum_j exp(\delta_{mjt}^r)] + \bar{\alpha}_m^v + \alpha_t^v. \tag{2.31}$$

where $\bar{\gamma}_1^v = \gamma_1^v \mathrm{P(Y)}$ and $\bar{\alpha}_p^v = [\gamma_1^v(1 - \mathrm{P(Y)})G_p + \alpha_p^v]$. Both $\mathrm{P(Y)}$ and $\ln[\sum_j exp(\delta_{jt}^r)]$

cannot be observed in the data. However, we can approximate δ^r_{jt} by the estimation results from equation 2.28 and estimate P(Y) by calculating the average patient request fulfill rate for each physician. Specifically, we have $\hat{\delta}^r_{jt} = \ln s^r_{kt} - \ln s^r_{0t} - \hat{\epsilon^r_{jt}}$ and $\hat{\mathrm{P}}(\mathrm{Y}) = \sum_{k',t} p^p_{k'|k',t}$. Finally, like the identification of DTCA and patient request, there are endogeneity concerns with respect to DTCA and patient visit decision. Again, border strategy is employed for these endogeneity concerns.

2.5.2 Demand Estimation Results

In this section, I present and discuss the estimation results of the demand model. The purpose of these regressions is to show whether or not pharmaceutical advertising affects patients and physicians as predicted by the demand model instead of accurately evaluating the magnitude of those effects. First, I discuss the summary statistics of the data used in estimation. Then, I display how patient requests affect physician prescription decisions in the anticholesterol market. Next, I quantify the impacts from DTCA on patient request decisions and how DTP advertising affects physicians' choices conditioning on patient request behaviors. Finally, I show the effects from DTCA on patients visit decisions.

Summary Statistics

Summary statistics for prescription, request, and DTP advertising data are presented in Table 2.6. The data were collected from 2956 physicians between January 1, 2007 and December 31, 2008. On average, each physician was observed for nearly 12 months [6]. The number of prescriptions written by each physician is about 12 per month, of which

[6] Physicians were enrolled in the data set on different dates, but they did not exit after enrollment.

15.8% are new prescriptions and the rest are prescription refills. Of the 2956 physicians, 26.9% had been requested to prescribe a specific brand by their patients, and the number of request per month is slightly greater than 1. More than half of the patients (52%) were covered by private health insurance and 34% were covered by Medicare and Medicaid. Of all patients in the data set, 8% were newly diagnosed with hyperlipidemia. Finally, on average, each physician received 5 detailing visits per month for a branded product, consuming 24 minutes of a physicians time in total.

Summary statistics for DTCA and demographic data are presented in Table 2.7. The data included 186 border areas from 93 DMAs in the US. On average, each branded product spent 1.7 cents per capita in each DMA. The variation in DTCA expenditures across markets and time was substantial even after controlling for the fixed effects used in regression (Figure 2.8). The average population across each DMA-border area within the sample period was 3 million, and the average number of physicians was about 900[7].

Patient Request and Prescription Choices

Equation 2.25estimates the impacts from patients' requests on physician prescription choices. To account for any possible differences in decisions to refill existing prescriptions, to write new prescriptions for previously treated patients, and to write new prescriptions for newly diagnosed patients, I separately report estimation results for the latter two subsamples.

The identification of θ_p requires observing the share of brand k and the outside option conditioning on brand k and the outside option being requested, which reduces the physician sample size to 5257 for the overall prescription regression. Although the

[7] Population size and physician number from counties bordering more than one DMA were included in calculations for all bordering areas.

number of observations used in the regression only account for a small portion of the data, these observations include prescription decisions made by 532 physicians, which is about 18% of all physicians surveyed by BrandImpactRx. Therefore, the estimation results should be reasonably representative.

The estimation shows that physicians value patient requests (Figure 2.13). Patient requests have positive and significant effects on overall prescription share for branded products (Table 2.8). On average, physicians value patients requests slightly less than their own perspective about medications (0.8 vs 1). The results are similar when I focus on new prescriptions for previously treated patients (Table 2.9) and on new prescriptions for patients who are newly diagnosed with hyperlipidemia (Table 2.10).

There are some variations in physicians' accommodation pattern across brands (Figure 2.14) and time (Figure 2.15). Specifically, physicians are more accommodating when patients request the new market entrant, Simcor (Figure 2.14). This finding is consistent with a previous finding that physicians are likely to experiment with new medications to learn from patients experiences (Chintagunta et al., 2012). In addition, physicians value patients requests more in later periods in the sample (Figure 2.15), which is consistent with an increased emphasis on shared clinical decision making in recent years.

DTCA and Patient Request

Equation 2.28 estimates the effects of DTCA on patients' requests for branded products. Because patients past experiences with anticholesterol medications would affect their prescription request decisions, I separately identify how DTCA affects patients who take no anticholesterol medications before the physician visit (Table 2.13), patients who visit the physician for the first time but have been prescribed anticholesterol medications before the visit (Table 2.12), and the overall patient population (Table 2.11). In addition, because patients with different health insurance plans have different out-of-pocket costs and formulary options, they tend to have diverse reactions to DTCA. As a result, I distinguish between patients who have private healthcare insurance and patients who have Medicare and Medicaid insurance.

The estimation results show that DTCA significantly increases branded product requests from patients with private healthcare insurance but has little impact on patients who are covered by Medicare or Medicaid. Patients with private healthcare insurance tend to have lower copayments and more formulary options, which imply lower cost for more medication choices. Therefore, they are more likely to request a branded product. Finally, patients with new prescriptions for anticholesterol medications and patients newly diagnosed with hyperlipidemia are comparably reactive to DTCA when making brand request decisions as experienced patients

DTP Advertising and Prescription Choices

Equation 2.21 estimates how DTP advertising affects physicians prescription decisions, conditioning on patient requests. Specifically, I examine the effects from DTP advertising when patients request an outside option (Table 2.14 and 2.15) and when patients request competitors brands (Table 2.16 and 2.17). Consistent with previous research, DTP advertising, as measured by both number of detailing visits and weighted minutes spent on a given product, has a positive and significant effect on market share of detailed brands in both cases. The positive and significant effects remain when competitors' detailing efforts are included as a control variable (Table 2.18)

DTCA and Patient Visit

Finally, equation 2.31 estimates the impacts from DTCA on patient visit decisions. The result shows that higher inclusive value of advertised branded products results in more patient visits to physicians (Table 2.19). It implies that, overall, brand-specific DTCA expands the market for all brands in a medication class because it increases the inclusive value of all advertised products.

2.5.3 Synergistic DTCA and DTP Advertising

Given the demand estimation results, I qualitatively display the synergistic effects between DTCA and DTP advertising through simulation of a single-agent marketing problem. The profit function in the simulation is assumed to be:

$$\pi_{mkt} = MR_k s_v \sum_{k'} s^r_{k'} s^p_{k|k'} - c^1 \mathrm{DTP}_k - \mathrm{DTCA}_k,\ \ s.t:\ c^1\mathrm{DTP}_k + \mathrm{DTCA}_k \leqslant y.$$

where M refers to market size, R refers to mark-up per prescription, c^1 refers to the marginal cost of detailing visits, and y refers to the advertising budget. The values of these parameters are listed in table 2.21: I assume $M = 100$, $R = \$150$, $c^1 = \$100$, and $y = 1500$.

In the simulation, I first calculate the incremental profits when both DTCA and DTP advertising are used together than when either DTCA or DTP advertising is used alone by the pharmaceutical company for a given brand budget. Specifically, I compare the profits of the pharmaceutical company across the following five cases:

1. DTCA expenditure =1500, DTP advertising expenditure =0 (DTCA only)

2. DTCA expenditure =600, DTP advertising expenditure = 900 (DTCA focused)

3. DTCA expenditure =500, DTP advertising expenditure = 1000 (Benchmark)

4. DTCA expenditure =400, DTP advertising expenditure = 1100 (DTP focused)

5. DTCA expenditure =0, DTP advertising expenditure =1500 (DTP only)

I use the third marketing scheme, where DTCA expenditure =500, DTP advertising expenditure = 1000, as the benchmark across different scenarios. I first calculate the profit rate differences between the benchmark and the other four marketing schemes. Then I decompose the profit rate difference to explore where the synergistic effects come from and how they vary by the demand parameter values. Specifically, I examine by how much the share of patient visit, patient request, and physician's prescription choice can explain the differences in profit rate differences. I use π_1 to represent the profit of the benchmark, and π_2 to represent the profit of alternative marketing schemes:

$$
\begin{aligned}
\frac{(\pi_1-\pi_2)/\pi_2}{(\pi_1-\pi_2)/\pi_2} &= \frac{MRs_{v1}\sum\limits_{k'} s_{k'}^{r1}s_{k|k'}^{p1} - y - (MRs_{v2}\sum\limits_{k'} s_{k'}^{r2}s_{k|k'}^{p2} - y)}{\pi_1-\pi_2} \\
&= \frac{MR[(s_{v1}-s_{v2})\sum\limits_{k'} s_{k'}^{r1}s_{k|k'}^{p1} + s_{v2}\sum\limits_{k'}(s_{k'}^{r1}-s_{k'}^{r2})s_{k|k'}^{p1} + s_{v2}\sum\limits_{k'} s_{k'}^{r2}(s_{k|k'}^{p1}-s_{k|k'}^{p2})]}{\pi_1-\pi_0} \\
&= \frac{(s_{v1}-s_{v2})\sum\limits_{k'} s_{k'}^{r1}s_{k|k'}^{p1}}{s_1-s_2} + \frac{s_{v2}\sum\limits_{k'}(s_{k'}^{r1}-s_{k'}^{r2})s_{k|k'}^{p1}}{s_1-s_2} + \frac{s_{v2}\sum\limits_{k'} s_{k'}^{r2}(s_{k|k'}^{p1}-s_{k|k'}^{p2})}{s_1-s_2}
\end{aligned}
\tag{2.32}
$$

The first term in the last row of equation 2.32 measures the share of profit rate difference induced by the changes in a patient's physician visit decision. The second term measures the share of profit difference caused by the changes in a patient's brand request decision. The last term measures the share of profit difference induced by the changes in a physician's prescribing decision, conditioning on physician visit and brand request decisions.

Table 2.22 presents the simulation results. In the first scenario where parameter values are listed in Table 2.21, the marketing schemes that use both DTCA and DTP advertising strictly dominate the DTCA only and the DTP only schemes. In addition, within the three marketing schemes, the DTCA focused earns higher profit rate than the other two. Decomposition of the incremental profit rates shows that compared to physician visit, patient request is the primary channel through which DTCA increases profits. The combination of DTCA and DTP advertising dominates DTCA only and DTP only because: (1) Mathematically, the market share is a product of the visit share, the request share, and the physician share. The product would be larger when the three components are equally large than when they are not; (2) Economically, for the DTCA only case, the DTP advertising encourages physicians to prescribe the advertised product and the positive effects outweigh the negative impacts on physician visit and brand request associated with lower DTCA expenditure. Likewise, the combination of DTCA and DTP advertising dominates DTP advertising only because DTCA encourages patients to visit physicians and request the advertised brand, and the positive effects outweigh the negative impacts on physician prescription choices that are associated with lower DTP advertising expenditure.

Next, I examine how the synergistic effects would change with different demand parameters. First, when consumers become more responsive to DTCA, the combination of DTCA and DTP advertising become less dominant to DTCA only but more dominant to DTP advertising only. Likewise, the incremental profit rate of DTCA focused marketing scheme becomes larger. This finding is not unexpected because more responsive consumers lead to higher marginal benefits of DTCA. Conversely, the profit gap between the combination of DTCA and DTP advertising and DTP advertising alone shrinks as physicians become more responsive to DTP advertising, while the disadvantages of DTCA alone become larger. For the same reason, the profit rate gap between DTP focused marketing scheme and the benchmark case becomes smaller.

2.6 Discussion

2.6.1 Limitations of the Border Strategy

Similar to other regression discontinuity design, one main concern of the border strategy is whether or not the estimated treatment effects along the borders can be identified among the inward counties. However, the fact that the border counties have similar characteristics, such as average population, average income, average number of physicians, and average number of physicians as interior counties (Shapiro, 2017) might partially address this concern.

Another threat to the border strategy, particularly for the demand estimation results, is the potential for measurement error. Specifically, there are three types of measurement error that could bias the estimation results. First, patients might visit physicians operating in a different DMA; second, patients from bordering counties might visit physicians operating in an interior county of the same DMA; and third, patients might watch Internet-based programs or see programs broadcast from the DMA across the border. Because the bias induced by all these types of measurement error is downward, I interpret my estimation results based on the lower bounds of the true parameters.

Finally, due to data limitations, I omit price and copay in the demand estimation. Because medication prices across adjacent counties within a given quarter tend not to vary significantly, the product-border-quarter fixed effect is likely to absorb price variations. Likewise, for patients with the same type of insurance, the variations in their associated copay for the same product are likely limited and any variations are addressed by the product-border-quarter fixed effect.

2.6.2 Policy Implication

The identified strategic DTP advertising and DTCA and the ways they affect physicians and patients in the pharmaceutical industry have policy implications. For example, shall pharmaceutical DTCA be banned? Because pharmaceutical DTCA can drive demand for expensive branded products despite the existence of equivalent but much less expensive generic alternatives, the American Medical Association called for a ban on DTCA[8]. It is true that DTCA encourages patients to request advertised brands (Table 2.11), which could lead to higher healthcare expenditure but not necessarily better healthcare outcomes. However, DTCA also encourages patients to talk to their physicians about treatment options (Table 2.19), which could be beneficial as many diseases are underdiagnosed and/or undertreated (Iizuka and Jin, 2005). In addition, because DTCA and DTP advertising are strategically related (Table 2.1), banning DTCA would lead to lower DTP advertising. Because DTP advertising provides physicians with riskbenefit information for the advertised product, lowering DTP advertising might negatively impact physicians' acquisition of knowledge about a new product (Ching and Ishihara, 2012).

[8] AMA Calls for Ban on DTC Ads of Prescription Drugs and Medical Devices. https://www.ama-assn.org/content/ama-calls-ban-direct-consumer-advertising-prescription-drugs-and-medical-devices. Accessed November 20th, 2016.

Therefore, additional studies of the impact of DTCA on patients and its correlation with DTP advertising are needed.

2.7 Conclusion

Using data from the anticholesterol market, I find pharmaceutical companies make strategic DTCA and DTP advertising by using the border strategy. Specifically, a 10% increase in DTCA expenditure per capita is associated with 0.3%-0.4% more detailing visits or 1% more detailing time for a given product in a given market. The identified positive relationship between DTP advertising and DTCA is consistent with a documented synergistic effect between these two marketing tools (Narayanan et al., 2004). To further understand the source of the synergistic effect, I construct and estimate a demand model that explicitly models patients' and physicians' decisions about requesting and prescribing brand-name medications considering the impacts from pharmaceutical advertising. I find DTCA encourages patients to visit their physicians and encourages patients with private healthcare insurance to request the advertised brand; physicians value patients' request and are more likely to prescribe the requested brand; and DTP advertising boosts the number of prescriptions for the advertised brand, whether the brand is requested by the patient or not. Simulation results show that comparing to patient visit, patient request for a brand-name medication is the primary channel through which DTCA affects patients and is the source of the synergistic effect between DTCA and DTP advertising.

These findings have both advertising strategy and healthcare policy implications. Pharmaceutical firms might be able to realize more gains by coordinating DTCA and DTP advertising than if they fail to coordinate these efforts. Moreover, regulators should consider the connection between DTCA and DTP advertising when making policies, otherwise regulatory policies might lead to unintended or even opposing consequences.

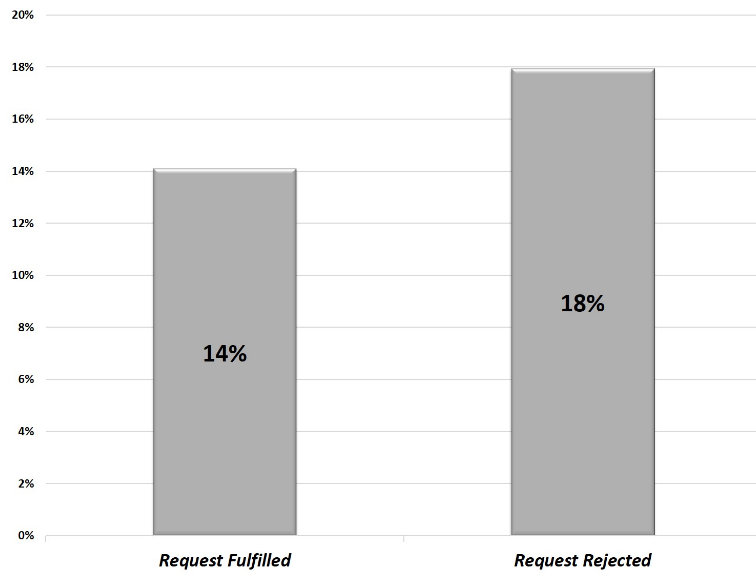


FIGURE 2.1: 32% of patients have had made a brand request and half of them were fulfilled by the physicians.

Source: Author's analysis using data from Kaiser Family Foundation.

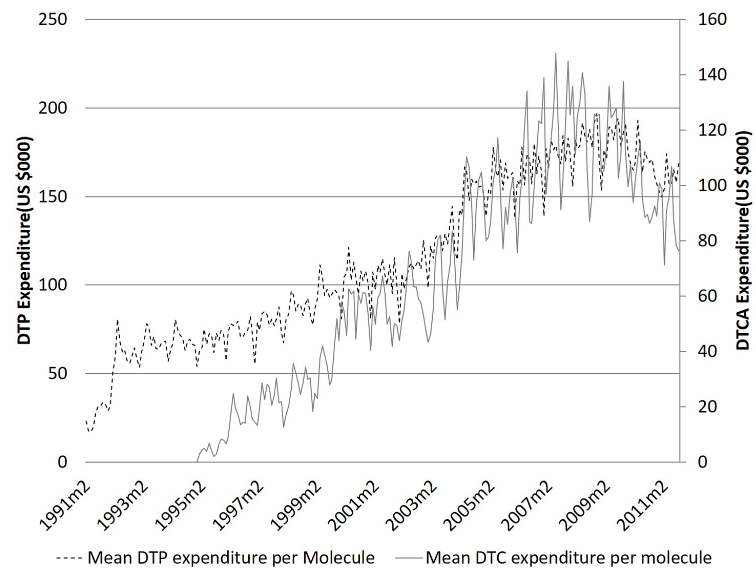


Figure 2.2: Direct-to-consumer advertising expenditure comoves with direct-to-physician advertising expenditure.

Source: Author's analysis using data from SDI Health.

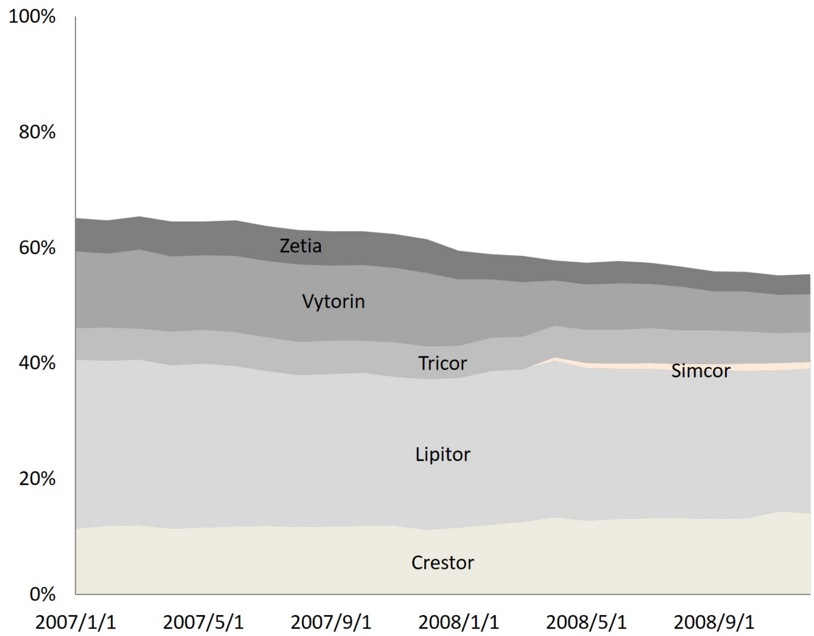


FIGURE 2.3: Share of prescriptions of branded anticholesterol medications from 2007 to 2008.

Source: Author's analysis using data from AlphaImpactRx.

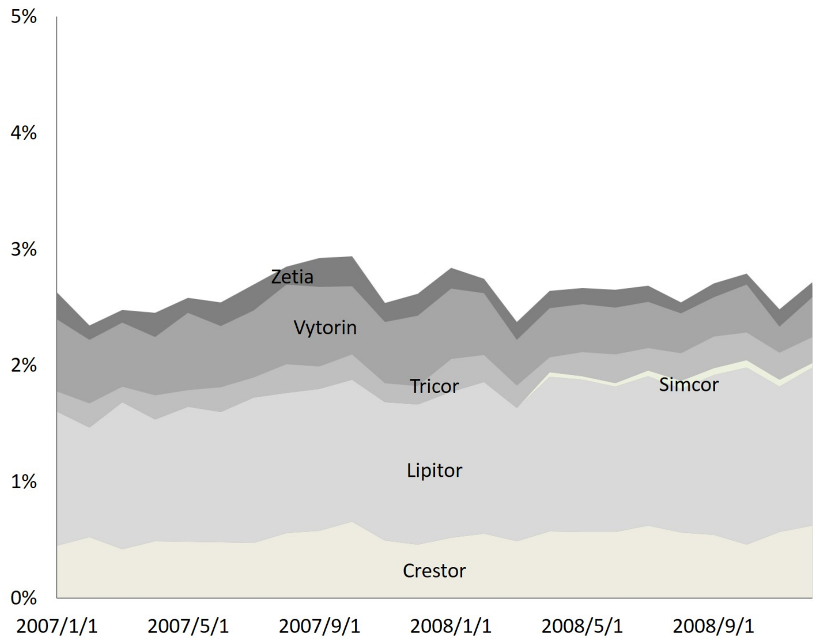


FIGURE 2.4: Share of patient request of branded anticholesterol medications.

Source: Author's analysis using data from AlphaImpactRx.

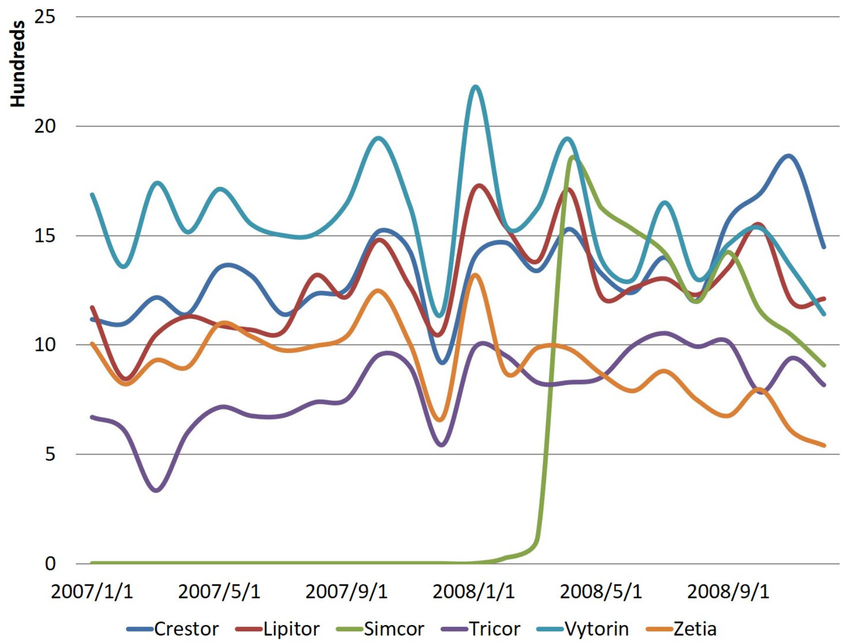


FIGURE 2.5: Number of detailing visits for branded anticholesterol medications.

Source: Author's analysis using data from AlphaImpactRx.

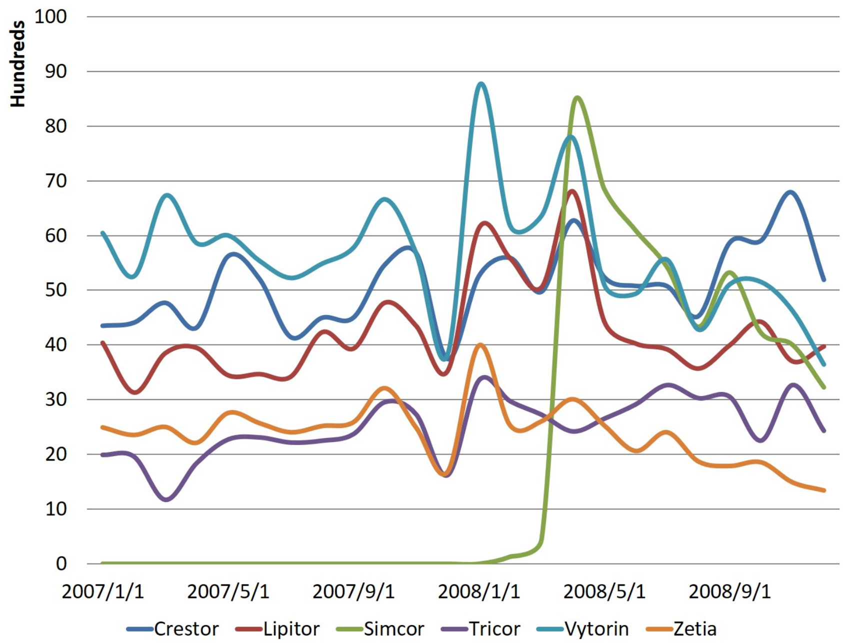


Figure 2.6: Number of detailing minutes for branded anticholesterol medications.

Source: Author's analysis using data from AlphaImpactRx.

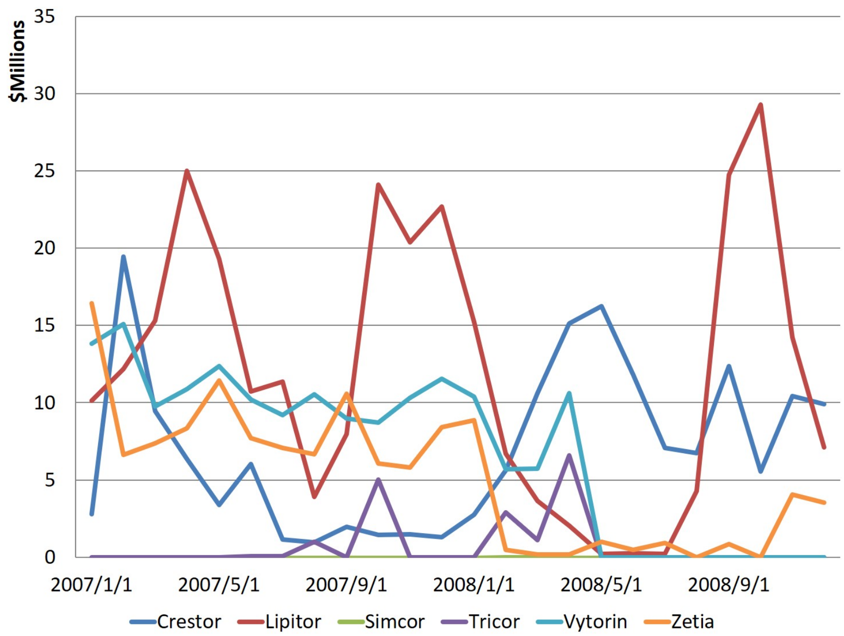


FIGURE 2.7: Direct-to-consumer advertising expenditures for branded anticholesterol medications from 2007 to 2008.

Source: Author's analysis using data from Ad$pender.

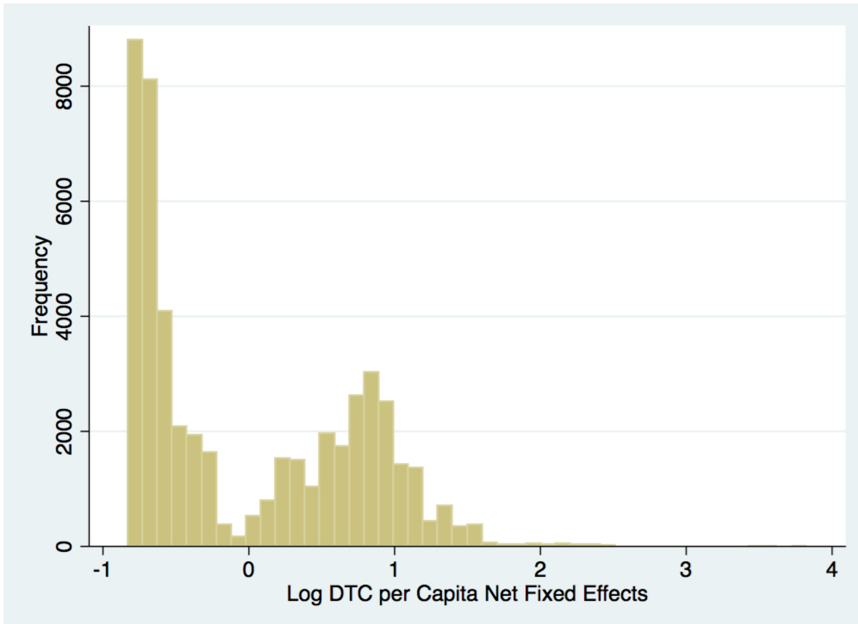


FIGURE 2.8: Substantial variations in log direct-to-consumer-advertising expenditure per capita net of fixed effects.

Source: Author's analysis using data from Ad$pender and 2008 population projections data from US Census Bureau

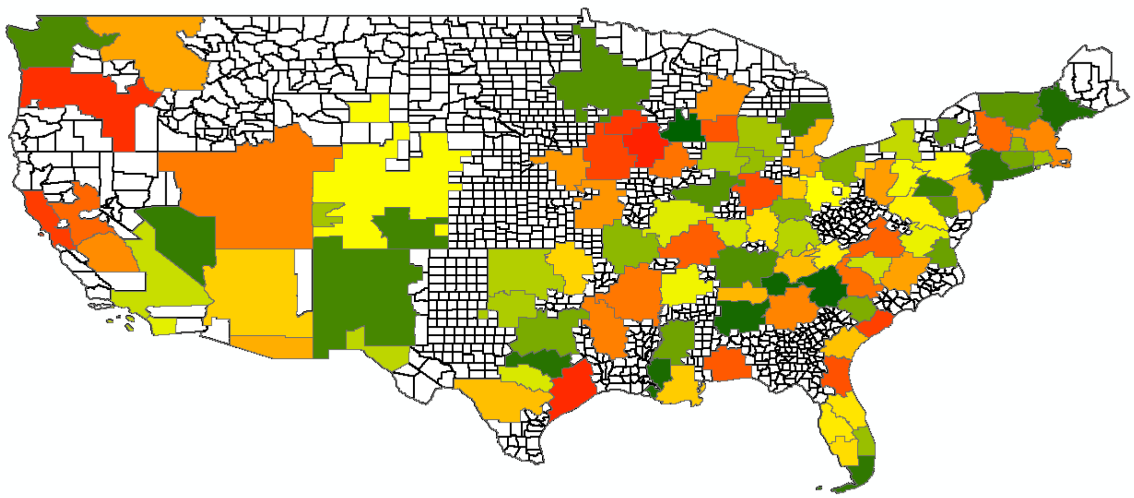


FIGURE 2.9: Top 101 DMAs in the US.

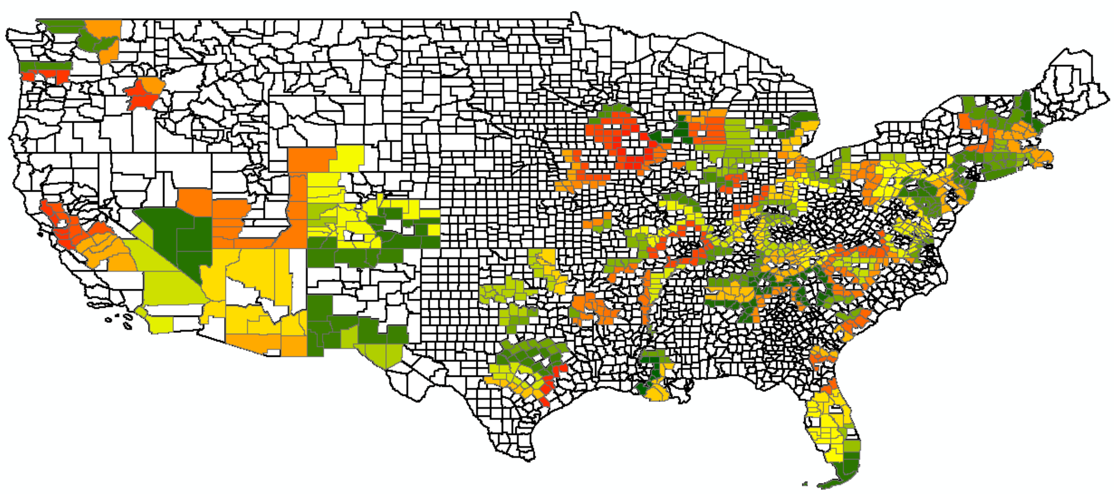


FIGURE 2.10: Counties along the border of the Top 101 DMAs in the US.

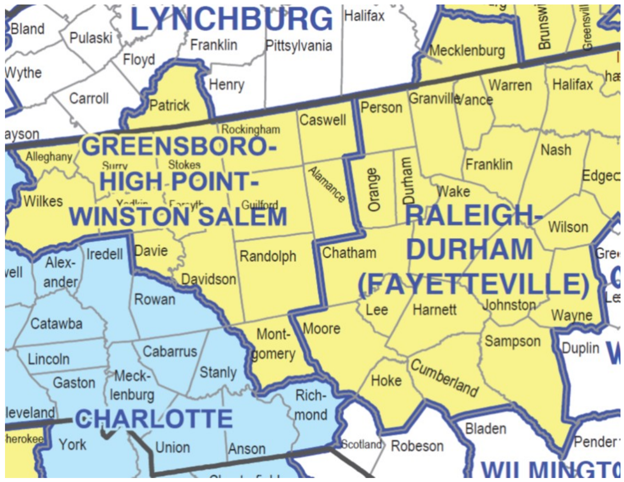
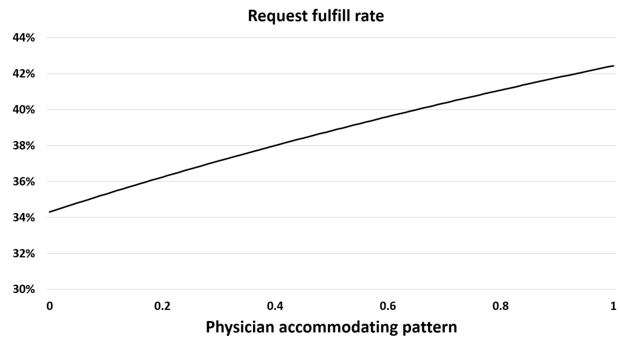
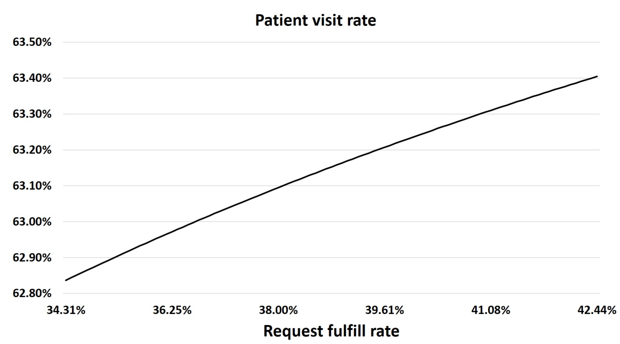


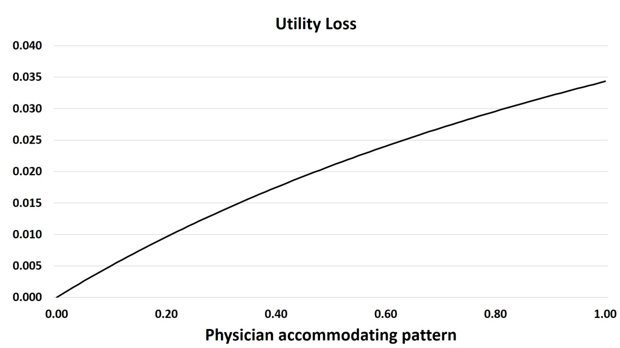
FIGURE 2.11: DMA examples in North Carolina.



(a) Brand request fulfill rate increases with physicians' accommodation pattern.



(b) Patient visit rate increases with brand request fulfill rate.



(c) Physicians' utility loss increases with accommodation pattern.

FIGURE 2.12: Simulated relationship between physician accommodation pattern, patient brand request fulfill rate, and patient visit rate.

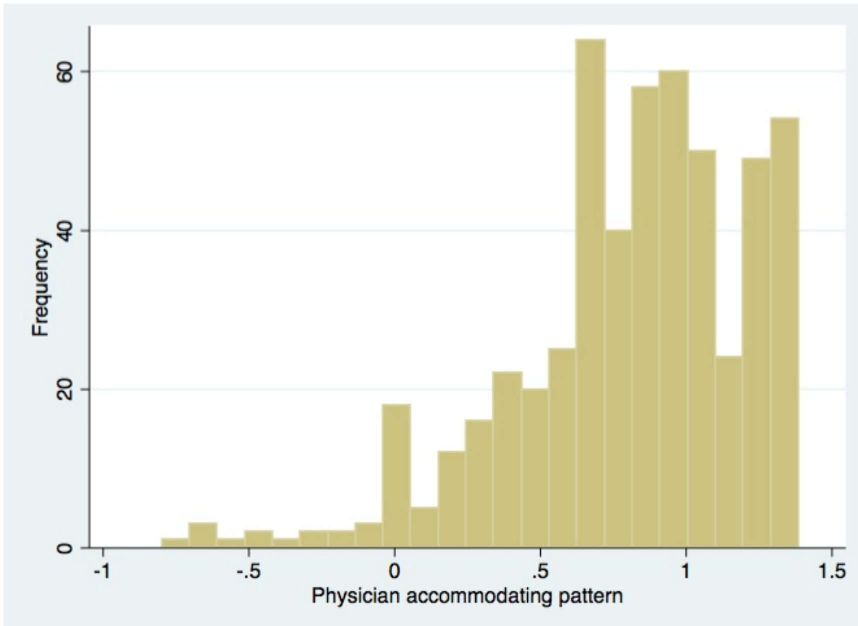


FIGURE 2.13: Distribution of physician accommodation pattern across physicians.

Source: Author's analysis using data from AlphaImpactRx

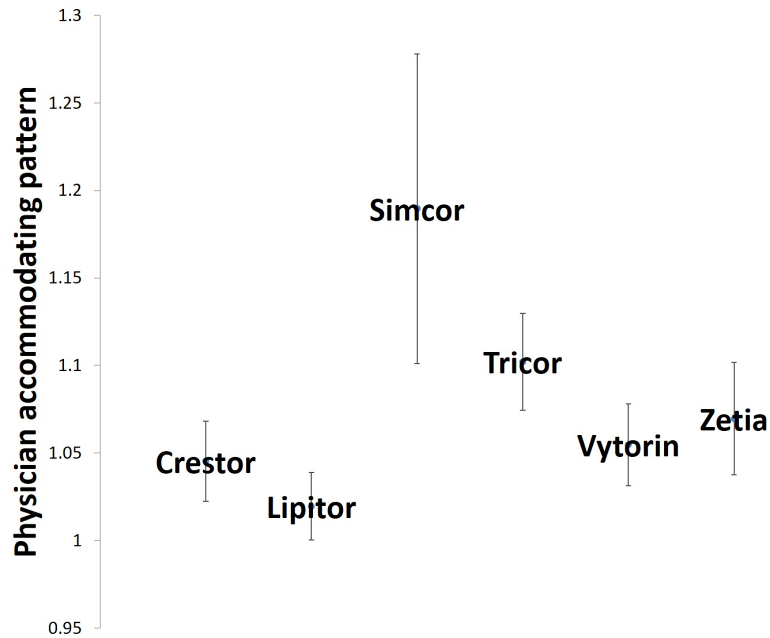


FIGURE 2.14: Distribution of physician accommodation pattern across brand.

Source: Author's analysis using data from AlphaImpactRx

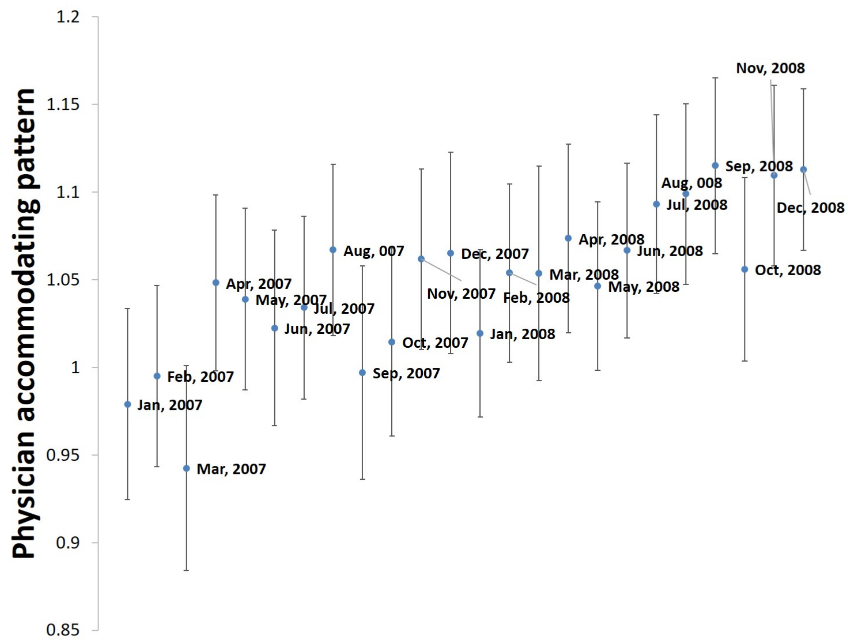


FIGURE 2.15: Distribution of physician accommodation pattern across time from 2007 to 2008.

Source: Author's analysis using data from AlphaImpactRx

Table 2.1: Coordinated DTCA and DTP advertsing, level.

	Detailing Visits$_{kmt}$	Weighted Detailing Minutes$_{kmt}$
DTC per Capita$_{kmt}$	0.040***	0.128***
	(0.008)	(0.032)
Brand-DMA-border fixed effects	x	x
DMA-border-quarter fixed effects	x	x
N	50844	50844
R^2	0.849	0.750

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.2: Coordinated DTCA and DTP advertising, logarithmic.

	Log Detailing Visits$_{kmt}$	Log Weighted Detailing Minutes$_{kmt}$
Log DTC per Capita$_{kmt}$	0.038***	0.058***
	(0.006)	(0.011)
Brand-DMA-border fixed effects	x	x
DMA-border-quarter fixed effects	x	x
N	50844	50844
R^2	0.831	0.767

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.3: Coordinated DTCA and DTP advertising with more controls, level.

	Detailing Visits$_{kmt}$	Weighted Detailing Minutes$_{kmt}$
DTC per Capita$_{kmt}$	0.028***	0.084***
	(0.008)	(0.033)
DTC per Capita$_{-k,mt}$	0.012***	0.106***
	(0.003)	(0.018)
DTC per Capita$_{km,t-1}$	0.007	0.031
	(0.005)	(0.028)
DTC per Capita$_{-k,m,t-1}$	0.001	0.018*
	(0.001)	(0.011)
Detailing$_{-k,mt}$	0.096***	0.050***
	(0.004)	(0.004)
Detailing$_{km,t-1}$	0.089***	-0.025
	(0.021)	(0.016)
Detailing$_{-km,t-1}$	-0.002	0.007
	(0.004)	(0.005)
Brand-DMA-border fixed effects	x	x
DMA-border-quarter fixed effects	x	x
N	48576	48576
R^2	0.864	0.757

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.4: Coordinated DTCA and DTP advertising with more controls, logarithmic.

	Log Detailing Visits$_{kmt}$	Log Weighted Detailing Minutes$_{kmt}$
Log DTC per Capita$_{kmt}$	0.029***	0.047***
	(0.006)	(0.012)
Log DTC per Capita$_{-k,mt}$	0.034***	0.062***
	(0.006)	(0.011)
Log DTC per Capita$_{km,t-1}$	0.006	0.002
	(0.007)	(0.013)
Log DTC per Capita$_{-k,m,t-1}$	-0.003	-0.0001
	(0.006)	(0.014)
Log Detailing$_{-k,mt}$	0.163***	0.102***
	(0.010)	(0.008)
Log Detailing$_{km,t-1}$	0.016	-0.063***
	(0.014)	(0.013)
Log Detailing$_{-km,t-1}$	0.049***	0.046***
	(0.005)	(0.006)
Brand-DMA-border fixed effects	x	x
DMA-border-quarter fixed effects	x	x
N	48576	48576
R^2	0.840	0.773

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.5: Branded anticholesterol drugs, 2007-2008

Brand	Molecule	Firm	Approval Date	Class
Crestor	Rosuvastatin	AstraZeneca	2003.08	Statins
Lipitor	Atorvastatin	Pfizer	1996.12	Statins
Simcor	Niacin/Simvastatin	Merck	2008.02	Statins
Tricor	Fenofibrate	Abbvie	2008.02	Fibric acid
Vytorin	Ezetimibe / Simvastatin	Merck	2004.07	Statins
Zetia	Ezetimibe	Merck	2002.10	Antilipemic

Source: Author's analysis using data from Drugs@FDA.

Table 2.6: Summary statistics of prescription and patient request

	N	**Std.**	**Min**	**Max**
# of Physician	2956			
% being Requested	26.9%			
% of New Prescriptions	15.8%			
% of Prescriptions for Newly Diagnosed Patients	8.01%			
% Private Health Insurance	52.3%			
% Medicare	34.3%			
# of Months	11.73	6.84	1	24
# of Prescriptions per Month	12.18	14.66	1	247
# of Requests per Month	1.09	6.04	0	80
# of Detailings Visits per Month	5.25	4.91	1	53
# of Detailings Minutes per Month	24.22	28.82	0.5	588

Source: Author's analysis using data from AlphaImpactRx.

Table 2.7: Summary statistics of DTCA, detailing, and demographic Information

	Mean	**SD**	**Min**	**Max**
Number of Border	186			
Number of DMA	93			
DTC_{kmt}	1.7	2.7	0	100.3
Population_{mt}	3.107	3.574	0.356	20.183
Number of Physicians_{mt}	891.908	1785.992	3	11183

Source: Author's analysis using data from AC Nielsen, Ad$pender, and US Census.

Table 2.8: How patient request affects physicians. All patients.

	θ_{pbt}	θ_p
Patient Request	1.049***	0.812***
	(0.005)	(0.018)
t-statistics	192.126	46.147
Observation	5257	532

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.9: How patient request affects physicians. New prescriptions only.

	θ_{pbt}	θ_p
Patient Request	0.881***	0.803***
	(0.016)	(0.029)
t-statistics	53.570	27.322
Observation	1205	321

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.10: How patient request affects physicians. Newly diagnosed patients only.

	θ_{pbt}	θ_p
Patient Request	0.955***	0.825***
	(0.022)	(0.043)
t-statistics	42.611	18.848
Observation	538	143

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.11: DTCA and brand request. All patients.

	Overll Prescription	
Variable	Non-private insurance	Private insurance
Log DTC PC $_{kmt}$	-.00002	0.002**
	(.0007)	(0.001)
Brand-DMA-border	x	x
Brand-border-quarter	x	x
N	42672	40290
R^2	0.774	0.652

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.12: DTCA and brand request. Patients with new prescriptions only.

	New Prescription	
Variable	Non-private insurance	Private insurance
Log DTC PC $_{kmt}$	0.0002	0.003**
	(0.001)	(0.001)
Brand-DMA-border	x	x
Brand-border-quarter	x	x
N	30192	29868
R^2	0.502	0.449

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.13: DTCA and brand request. Newly diagnosed patients only.

	Newly Diagnosed	
Variable	Non-private insurance	Private insurance
Log DTC PC $_{kmt}$	0.0003	0.004*
	(0.003)	(0.002)
Brand-DMA-border	x	x
Brand-border-quarter	x	x
N	18972	22632
R^2	0.537	0.497

Standard errors in parentheses are clustered at DMA-border level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.14: DTP advertising and prescription choice. Number of detailing visits.

	Version 1	Version 2	Version 3	Version 4
Log Detailing$_{kpt}$	0.011***	0.006***	0.005***	0.005***
	(0.002)	(0.001)	(0.001)	(0.001)
Brand-time fixed effects	x	x		
Physician-brand fixed effects	x	x	x	x
Physician-time fixed effects		x	x	x
MSA-brand-time fixed			x	
ZIP3-brand-time fixed				x
Observations	243784	239636	210667	195870
R^2	0.527	0.922	0.931	0.939

Standard errors in parentheses are clustered at physician level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.15: DTP advertising and prescription choice. Weighted detailing minutes.

	Version 1	Version 2	Version 3	Version 4
Log Detailing	0.005***	0.003***	0.002***	0.002***
Weighted Minutes$_{kpt}$	(0.001)	(0.000)	(0.000)	(0.000)
Brand-time fixed effects	x	x		
Physician-brand fixed effects	x	x	x	x
Physician-time fixed effects		x	x	x
MSA-brand-time fixed			x	
ZIP3-brand-time fixed				x
Observations	243784	239636	210667	195870
R^2	0.527	0.922	0.931	0.939

Standard errors in parentheses are clustered at physician level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.16: DTP advertising and prescription choice when competitor brand is requested. Number of detailing visits.

	Version 1	Version 2	Version 3	Version 4
Log Detailing$_{kpt}$	0.006**	0.004**	0.007*	0.005*
	(0.003)	(0.002)	(0.001)	(0.003)
Brand-time fixed effects	x	x		
Physician-brand fixed effects	x	x	x	x
Physician-time fixed effects		x	x	x
MSA-brand-time fixed			x	
ZIP3-brand-time fixed				x
Observations	28577	28577	21331	19905
R^2	0.297	0.602	0.546	0.546

Standard errors in parentheses are clustered at physician level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.17: DTP advertising and prescription choice when competitor brand is requested. Weighted detailing minutes.

	Version 1	Version 2	Version 3	Version 4
Log Detailing	0.003***	0.002***	0.004**	0.004**
Weighted Minutes$_{kpt}$	(0.001)	(0.002)	(0.001)	(0.001)
Brand-time fixed effects	x	x		
Physician-brand fixed effects	x	x	x	x
Physician-time fixed effects		x	x	x
MSA-brand-time fixed			x	
ZIP3-brand-time fixed				x
Observations	28577	28577	21331	19905
R^2	0.297	0.602	0.569	0.546

Standard errors in parentheses are clustered at physician level

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Source: Author's analysis using data from AlphaImpactRx.

Table 2.18: DTP advertising and prescription choice after controlling DTP advertising from competitors. Number of detailing visits.

	Version 1	Version 2	Version 3	Version 4
Log Detailing$_{kpt}$	0.010***	0.004***	0.004**	0.005**
	(0.001)	(0.001)	(0.001)	(0.002)
Log Detailing$_{-k,pt}$	0.005**	-0.004^{+}	-0.003	-0.001
	(0.002)	(0.002)	(0.003)	(0.003)
Brand-time fixed effects	x	x		
Physician-brand fixed effects	x	x	x	x
Physician-time fixed effects		x	x	x
MSA-brand-time fixed			x	
ZIP3-brand-time fixed				x
Observations	243784	239636	210667	195870
R^2	0.527	0.922	0.931	0.939

Standard errors in parentheses are clustered at physician level
$^{+}$ $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
Source: Author's analysis using data from AlphaImpactRx.

Table 2.19: DTCA leads more patients to visit physicians.

	Overll Prescription
Inclusive Value$_{mt}$	0.002**
	(0.001)
Brand-DMA-border fixed effects	x
Border-quarter fixed effects	x
N	8232
R^2	0.938

Standard errors in parentheses are clustered at DMA-border level
* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$
Source: Author's analysis using data from AlphaImpactRx, Ad$pender, and US Census.

Table 2.20: Synergistic DTCA and DTP advertising, a simulated example

Marketing Scheme	Expenditure		Simulated Profits ($)
DTP and DTCA	DTP	750	353,260
	DTCA	600	
DTP only	DTP	1350	353,116
DTCA only	DTCA	1350	352,389

Table 2.21: Synergistic DTCA and DTP advertising, parameters

Parameters	Value
γ_1^v	0.002
γ_1^c	0.001
γ_1^p	0.003
θ^p	0.802
R	150
c^1	100
M	100
y	1500

Table 2.22: Synergistic DTCA and DTP advertising, simulation

Marketing Scheme ($)		Incremental	Decomposition		
DTCA	DTP	Profit Rate	Visit	Request	Physician
500	1000	0			
1500	0	-0.13%	0.25%	229.29%	-329.54%
600	900	0.03%	0.17%	157.14%	-57.31%
400	1100	-0.04%	-0.15%	-138.99%	39.14%
0	1500	-0.50%	-0.12%	-113.95%	14.07%
More responsive patients($\gamma_r = 0.0012$)					
500	1000	0			
1500	0	-0.07%	0.86%	819.04%	-919.90%
600	900	0.04%	0.15%	143.44%	-43.59%
400	1100	-0.05%	-0.14%	-130.48%	30.62%
0	1500	-0.61%	-0.12%	-110.55%	10.67%
More responsive physicians($\gamma_p = 0.006$)					
500	1000	0			
1500	0	-0.58%	0.06%	53.09%	-153.14%
600	900	0.01%	0.40%	375.05%	-275.46%
400	1100	-0.02%	-0.25%	-230.49%	130.74%
0	1500	-0.42%	0.14%	132.93%	-33.08%

3

Strategic Interaction among Governments in the Provision of a Global Public Good

3.1 Introduction

Knowledge generated by a firm's research and development (R&D) activities can be a public good, limiting the ability of the firm to fully appropriate the benefits of its investment (Bloom et al., 2013). As a result, firms tend to invest less money than is socially optimal. To correct for the market failure, governments use patents, innovation prizes, R&D tax credits, and direct funding of R&D through grants. The resulting innovation or knowledge can cross national borders, potentially causing other governments to alter their own innovation policies. We examine whether spending on basic medical research by one government affects spending by others. Economic theory suggests that it should (Olson and Zeckhauser, 1966; Lee, 1988; Nordhaus, 2015), but we have little evidence for this phenomenon outside of national defense spending (Murdoch and Sandler, 1984; Sandler and Murdoch, 1990) and environmental regulation (Murdoch and Sandler, 1997).

This is the first economic analysis to investigate whether governments respond strategically to one another in funding basic medical research. We focus on infectious and parasitic diseases because of the enormous impact of the diseases on human welfare.[1] We have data on research funding for 15 infectious and parasitic diseases across 41 countries and organizations from 2007 to 2014 collected annually by the non-profit Policy Cures. We are not aware of a similarly comprehensive source of medical research funding data for other diseases.

Identifying a strategic response by a funder is not straightforward. Two funders might experience the same economic shock to their budgets and adjust funding in the same direction. Also, two funders might prioritize the same diseases if they both consider disease burden or scientific productivity. To identify a strategic response, we need an exogenous shock to one budget to observe the response by other funders. We use the composition of United States (US) Congressional appropriations committees as an instrumental variable to address the endogeneity of government research funding. The US National Institutes of Health (NIH) accounted for more than half of global government and non-profit research funding for infectious and parasitic diseases between 2007 and 2014. Congress sets the NIH budget annually, and the budget fluctuates as the composition of Congress changes. When Congressional appropriations committees have more members representing research-intensive universities, US government research outlays tend to be higher. This exogenous change allows us to test whether other governments

[1] Infectious diseases were four of the top five priorities (nutrition being the fifth) for the Copenhagen Consensus III of 2012, during which an expert panel, including four Nobel laureates, set priorities for advancing global welfare (`http://www.copenhagenconsensus.com/copenhagen-consensus-iii/outcome`). Furthermore, with a philosophy of every life having equal value and of evidence-driven investment, the Gates Foundation – the largest in the world – spends most of its resources on medical care, especially in the infectious and parasitic disease areas.

adjust their spending in response.

We find that a 10 percent increase in US government outlays for medical research is associated with a 2 to 3 percent decrease in outlays by other funders (i.e., other government agencies or non-governmental organizations [NGOs]) in the following year. We also find that changes in US funding for a given disease typically influence other funders only if the other funders are already funding the disease. Government agencies tend to fund diseases with a high local burden and respond to US outlays more intensely for such diseases. In contrast, it is rare for a government agency to stop funding a disease entirely in response to an increase in US outlays, or begin funding a new disease in response to a decrease in US outlays. In other words, changes in US outlays primarily affect the intensive margin rather than the extensive margin for other funders.

The negative relationship between US government funding for a disease and funding by other governments, NGOs, and foundations is consistent with free riding. According to the World Health Organization:

"Failure to provide global public goods is linked to collective action problems such as 'free-riding.' The free-rider term describes a situation when no individual is prepared to pay the cost of something that others may be expected to benefit from; instead, all hope that someone else will pay for it and they will benefit for free. This is particularly an issue for research and development (R&D) into medicines to combat neglected diseases, which requires high-levels of investment."(World Health Organization, 2016)

Free riding is not the only explanation for this relationship, however. A negative relationship in funding outlays is also consistent with optimal reallocation. We cannot distinguish between the two. Regardless of whether we refer to it as free riding, optimal reallocation, or crowding out, it is important to be aware that when the US government increases outlays for research on a disease by one dollar, the global increase (net of foreign reductions) is smaller. We estimate an increase in net international outlays of \$.70 to \$.80 when the US government allocates one additional dollar to research on a disease.

3.2 Related literature

US drug makers and government officials sometimes complain that when other countries cap drug prices, they are free riding on the US market (Scherer, 1993). They argue that high prices in the US provide the demand that encourages much commercial drug development. However, despite largely unregulated drug prices, US-based firms or inventors are not disproportionately responsible for new molecular entities (Keyhani et al., 2010). However, with low trade and knowledge barriers, the location of invention may be irrelevant. What matters, rather, is the global profit potential that a firm expects, and this should not depend on the country in which the firm has its headquarters or operates a research laboratory.

The potential for free riding is one justification for the expansion of intellectual property requirements in international trade agreements; that is, each country would prefer other countries to provide patent protection to induce innovation. While intellectual property rights can reduce free riding and improve patient welfare in the long run, patient welfare can diminish in the short run due to rising drug or vaccine prices (Chaudhuri et al., 2006), especially for new products with little competition (Duggan et al., 2016). Furthermore, even diseases prevalent around the world will not receive much commercial investment if nearly all of the people suffering from the diseases live in poor countries (Kyle and McGahan, 2012). Intellectual property rights might be ineffective as an incentive mechanism to support medical research funding for such diseases, and thus motivate government, NGO, or foundation research funding. In contrast to discussion about intellectual property rights, there has been relatively little discussion of how national policies on research funding may be subject to free riding or require coordination. This is the first study to examine strategic interaction among governments in funding basic medical research.

Government R&D funding has been shown to crowd out *private* investment. Government R&D funding can crowd out private funding if government funding bids up the wages of scientists and engineers, which makes private investment in innovation more expensive (Goolsbee, 1998). Conversely, government funding can complement private investment if governments invest in early-stage research, while private investors fund later-stage development (Toole, 2007; Blume-Kohout, 2012). The complementarity of government research and private development for medical research funding has been more evident for early stage (Phase I) clinical trials rather than later, costlier (Phase III) trials (Blume-Kohout, 2012). However, it is difficult to find a clean econometric experiment to identify these effects (David et al., 2000).

In addition to investment crowd out, government funding may affect private charity spending (Andreoni and Payne, 2011). During the Great Depression, government charitable programs expanded, while private charities reduced funding for the poor and instead devoted funding to other causes (Roberts, 1984; Gruber and Hungerman, 2007). Murray (2013) recommended that governments consider the role of charities in scientific funding: "In determining their own funding strategies, they must no longer assume that their funding is the only source in shaping some fields of research while recognizing that philanthropy may ignore other important fields." Outside of medical research, previous work has examined how government funding affects the private provision of health insurance. Private health insurance coverage fell following the Medicaid expansions between 1987 and 1992 (Cutler and Gruber, 1996) and between 1996 and 2002 (Gruber and Simon, 2008). With public provision of health insurance, a smaller share of employees adopted employer-based insurance, and employers were less generous in providing insurance.

Governments also interact strategically at the local and state levels (Brueckner, 2003). Spending across neighboring state governments is positively correlated, perhaps due to herding (Case et al., 1993). Furthermore, tax policy is positively correlated between neighboring local governments due to competition for mobile capital (Mintz and Tulkens, 1986). In contrast to the positive correlation found in these contexts, we find a negative correlation in spending across governments when accounting for endogeneity, suggesting that R&D spending is a public good.

Although medical research is supplied and used globally, most previous studies have focused on NIH funding because the NIH is the largest funder of US medical research and because the US government makes NIH data available. However, one shortcoming of analyzing only NIH data is the possibility of biased estimates depending on whether other public spending is positively or negatively correlated with NIH funding outlays. If other governments devote resources to diseases in a pattern similar to that of the NIH, and if we omit the contribution of funding from other governments, then we will overestimate the effect of NIH spending. However, if an increase in spending by the NIH for a particular disease triggers a reduction by other public funders, then we will underestimate the effect of NIH spending. Scientific research is global and scientific efforts across countries surely influence one another, either as complements or substitutes. For example, when the George W. Bush administration prohibited federal funding for the development of and research on new human embryonic cell lines, US researchers increased collaboration with international researchers (Furman et al., 2012). One implication of our paper is to highlight the importance of accounting for strategic interactions when assessing the productivity of research funding in a single country.

3.3 Theory

Governments and foundations allocate R&D funding based on health needs and scientific opportunity. According to NIH leaders, "NIH believes that a process that includes multiple measurements of public health needs, but is also informed by scientific opportunity, allows us to fund the best science" (Rockey and Wolinetz, 2015). Hence, we model outlays as a function of disease burden and scientific knowledge (Lichtenberg, 2001).

We extend the previous framework by including multiple funders and a strategic response by smaller funders to the largest funder. For example, a European government funder might consider outlays by the NIH when choosing to fund a given disease. After all, knowledge generated by NIH-funded research is generally not restricted to the US population, because NIH policy requires recipients of NIH grants to make their papers available at no cost to the public.[2]

Funder f chooses outlays x_d^f for disease d based on the disease burden that can be alleviated B_d^f, scientific knowledge S_d, and the funder's budget Y^f. A funder distributes outlays between research that benefits people globally x_d^f and outside activities that are strictly local to the funder o^f. The probability of developing a new treatment is $p(\sum_f x_d^f, S_d)$ which is increasing in scientific knowledge S and concave in the outlay x.[3]

[2] See NIH Public Access Policy

[3] We assume funders have the same scientific productivity for the same disease regardless of which

The expected benefit to funder f of outlay x_d^f is the probability of discovery p multiplied by the disease burden alleviated B_d^f. The benefit to a funder includes other funders' outlays, but not other funders' disease burdens. Therefore, the optimization problem for a funder is:

$$\begin{aligned} &\max_{x_d^f} \sum_d B_d^f p(x_d^f, S_d) + h(o^f) \\ &s.t.: \sum_d x_d^f + o^f = Y^f \end{aligned} \tag{3.1}$$

In the appendix (section B), we employ a simple model with two periods and two funders, one of which is a dominant funder (for example, the NIH). We solve for comparative statics and generate three testable hypotheses.

We predict that outlays will be positively correlated with disease burden and scientific knowledge, though outlays will not necessarily be proportional to disease burden and scientific knowledge.

Hypothesis 5. *Diseases tend to receive greater outlays from a funder if there is a greater disease burden, if there is more scientific knowledge, and if the funder has a larger budget.*

Formally, $\partial x_d^{f*}/\partial B_d^f > 0$, $\partial x_d^{f*}/\partial S_d > 0$, and $\partial x_d^{f*}/\partial Y^f > 0$.

The remaining hypotheses concern how outlays by one funder influence funding by another funder.

funder it is. Approximately 90 percent of the outlays in our sample come from the US, the United Kingdom (UK), and France, and we think it is a reasonable assumption for this set of countries. Our assumption may be less valid for countries with a more limited pool of scientific talent.

Hypothesis 6. *Greater outlays for a disease by one funder will reduce outlays for the disease by another funder.*

Formally, for dominant funder f and a fringe funder i, $\partial x_d^{f*}/\partial x_d^{i*} < 0$. If the dominant funder increases outlays for a disease, fringe funders reduce outlays. The fringe funders spend more on other diseases and on the local (outside) good as described below.

Hypothesis 7. *Greater outlays for a disease by one funder increase outlays by the other funder for other purposes, including other diseases and the local (outside) good.*

Formally, $\partial x_{d'}^{f*}/\partial x_d^{i*} > 0$ and $\partial x_o^{f*}/\partial x_d^{i*} > 0$. When the dominant funder increases funding for a disease and the other funder reduces funding (Hypothesis 6), some of the funding goes to the local (outside) good and we might characterize it as free riding. However, some of the funding goes to other diseases. Hence, if the dominant funder "over funds" a disease (perhaps due to political pressure), then other funders shift resources to other diseases.

These three hypotheses motivate our empirical examination. One of our challenges is that there could be positive correlation in outlays across funders due to unobserved factors such as taste or mismeasurement in our disease burden and scientific knowledge data. We need a shock to one funder's budget to motivate this funder to change its outlays (Hypothesis 5) so that we can observe the change in the other funder's outlays (Hypothesis 6). We will not directly estimate whether governments are maximizing social welfare, but we will demonstrate how governments respond to one another.

3.4 Methods

Our unit of observation is a disease-funder-year. The model includes both US and global disability-adjusted life years (DALYs) as measures of disease burden, as well as scientific publications. Recall that NIH leaders wrote that "NIH believes that a process that includes multiple measurements of public health needs, but is also informed by scientific opportunity, allows us to fund the best science." Furthermore, "NIH funding levels relate to US and global deaths and disability-adjusted life years (DALYs) – a measure that quantifies the number of healthy years of life lost due to morbidity or premature mortality caused by disease" (Rockey and Wolinetz, 2015).

3.4.1 Identification

Two factors bias against finding a negative relationship between outlays across funders. The first identification challenge is that if the same unobserved factors motivate funders, then outlays across funders might move together. We control for common drivers, such as scientific publications, global burden of a disease, and national income. However, unobserved factors could motivate greater spending by both US and non-US funders. We need an instrumental variable that shifts US funding for a given disease in a given year but that does not directly change funding by non-US agencies, only affecting their funding indirectly through US funding.

Our instrumental variables strategy uses the political composition of the US Congress, which sets the overall NIH budget in addition to setting other global health priorities.[4] Changes in Congressional committee chairmanships influence total federal spending (Cohen et al., 2011). Likewise, Congressional representation affects medical research fund-

[4] See Yamey et al. (2017) for an overview.

ing. Previous work has documented the importance of academic earmarks, which are budgetary carve-outs by members of Congress directed to specific institutions located in their districts (de Figueiredo and Silverman, 2006). Researchers located in districts represented by members of the US House Appropriations Committee received more NIH grants than those without such representation (Hegde and Mowery, 2008; Hegde, 2009).[5]

The validity of our approach rests on the assumption that US political forces that shift NIH funding through changes in the composition of Congressional appropriations committees are unrelated to funding decisions in other countries. That is, the appointment to the House appropriations committee of a representative from a state with a large number of research-intensive universities (who then argues for a larger NIH budget to benefit the local constituency) is independent of the budgetary and funding choices in other countries. If our approach does not adequately address the identification challenge, then our estimates will underestimate the negative correlation and thus the strategic response of non-US funders. For example, if all countries change political control in the same direction, then funding across countries will be positively correlated. Hence, our estimates could be a lower bound.

The second identification challenge is that many funders have small budgets. They often spend nothing on a given disease and thus are limited in how they can respond to an increase in US outlays for that disease (i.e., they cannot spend less than zero). We therefore include a specification that focuses on the intensive margin, or changes

[5] A "committee on committees" for each party determines membership on Congressional committees. The committee gives priority to more senior members. New members are given priority according to past service in Congress or as governor. Other new members are sorted by random drawing. Members are generally not permitted to serve on multiple powerful committees. For example, a Senator serving on the Appropriations committee would give up her position in order to receive a position on the Armed Services committee. The committee membership recommendations are voted on within the party, and then in a simple resolution by all members.

conditional on spending anything, as well as a specification that looks only at the decision to allocate any funding at all. Again, our estimates might underestimate the effect and be a lower bound.

3.4.2 Estimation

We estimate outlays from a non-US funder f for a disease d in year t with the following specification:

$$\begin{aligned}
\text{Log Non-US Funder Outlay}_{d,f,t} \quad = \quad & \beta_0 + \beta_1 \text{Log US Outlay}_{d,t-1} \\
& \beta_2 \text{Log Local Disease Burden}_{d,c,t} + \\
& \beta_3 \text{Log Disease Burden in Poor Countries}_{d,t} + \\
& \beta_4 \text{Infectious except HIV}_d + \beta_5 \text{HIV Indicator}_d + \\
& \beta_6 \text{Log Number of Publications to Date}_{d,t} + \\
& \beta_7 \text{Log GDP}_{c,t-1} + \phi_f + \epsilon_{d,f,t}
\end{aligned} \tag{3.2}$$

The explanatory variables include the disease burden, scientific knowledge, and other control variables. The burden of disease in poor countries is net of the local burden for the disease, where poor countries are defined as those listed as low income and lower-middle income by the World Bank.[6] We measure scientific knowledge as the number of scientific publications to date. We also control for whether the disease is infectious or parasitic. Because HIV is unique in its global and rich-world disease burdens, as well as the medical research funding it has received, we include a separate indicator for HIV.

[6] `http://data.worldbank.org/country`

Finally, we include a funder fixed effect to account for time-invariant heterogeneity across funders.

Our main variable of interest is lagged US funding, which might depend on unobserved factors that also drive non-US funding decisions, as discussed previously. We address this endogeneity using two-stage least squares, where the first stage is:

$$\begin{aligned}
\text{Log US Outlay}_{c,t,d} \quad = \quad & \alpha_0 + \alpha_1 \text{Research Universities per Appropriations Member}_{t-2} \\
& + \alpha_2 \text{Log Local Disease Burden}_{d,c,t} \\
& + \alpha_3 \text{Log Disease Burden in Poor Countries}_{d,t} \\
& + \alpha_4 \text{Infectious except HIV}_d + \alpha_5 \text{HIV Indicator}_d \\
& + \alpha_6 \text{Log Number of Publications to Date}_{d,t} \\
& + \alpha_7 \text{Log GDP}_{c,t} + \phi_f + \epsilon_{d,c,t}
\end{aligned} \tag{3.3}$$

In the first stage, the dependent variable is the annual US outlay for disease d in year t. We transform the dependent variable into logs (plus one because many of the observations are zero). The instrumental variables we exclude from the second stage are the number of research-intensive universities represented by Congressional appropriations committee members.

The assumed timing in our analysis is as follows. The composition of the Congressional appropriations committees in year t influences the NIH budget in the next fiscal year, $t+1$. Researchers submit proposals and the NIH selects recipients, with allocations beginning in $t+2$. Other governments observe the NIH budget and funding decisions in

$t+1$, choose recipients for their funding in $t+2$, and make outlays in $t+3$.

We also estimate alternative specifications. In one specification, we include not only other non-US government agencies but also NGOs and private foundations. The approach is the same as that described above, except with more observations. In another specification, we add an interaction term between the local disease burden and US outlays. In this way, we examine whether government agencies were more responsive to US outlays for diseases with a heavy local burden. This allows us to use the heterogeneity in disease burden across countries to examine responses to US outlays at the intensive margin. To examine responses at the extensive margin, we replace the magnitude of a government agency's outlays with an indicator variable for whether the agency has any outlay for that disease. We include five other specifications to test the robustness of our results. We describe the robustness checks in Section 3.6.3 and include the tables in the appendix.

3.5 Data

To study how governments interact in medical R&D outlays, we need data on outlays by multiple government agencies, NGOs, and foundations for each disease and year. Although the NIH provides a long time-series of funding at the project level, collecting similar information from funders in other countries is challenging. Fortunately, Policy Cures collects and classifies funding outlays by disease, as described below. We also include data on the burden of disease at the country level, and data on scientific knowledge for each disease. We use data on the composition of Congressional appropriations committees as a source of exogenous variation in US outlays.

3.5.1 *Funding data*

We focus on infectious and parasitic diseases[7] because of the availability of high-quality data on funding from all relevant governments and foundations. Policy Cures collects the G-FINDER data using an annual survey. The survey covers public (government) and private (foundation and NGO) funding for 35 neglected diseases, including both infectious and parasitic diseases that predominantly affect people in developing countries. The annual survey defines neglected diseases as those for which treatments are needed in developing countries and for which the commercial market is insufficient to attract R&D spending by private industry.

Each record in the G-FINDER database includes the disease name, product category, funder name, funder type, home country of the funder, funding amount, year, and recipient information. A key contribution of the annual survey is that it allows a more accurate classification of spending by disease than a survey based on keywords. Furthermore, the G-FINDER database avoids double counting, such as funding that flows from the Gates Foundation to another organization, which then funds research. For more details on the G-FINDER data, see previous studies such as Moran (2010) and Røttingen et al. (2013).

We aggregate the G-FINDER data to the disease-funder-year level and adjust all outlays to 2013 US dollars. We set the outlay to zero for any disease-country-year and disease-funder-year that is missing in the G-FINDER database, so the data are fully

[7] Infectious and parasitic diseases are of interest for many reasons, not only because of the availability of data. First, these diseases are neglected by the private sector, because the disease burden is concentrated in poor countries, where the profits are low (Kremer, 2002). The case for government intervention is strong, because the social burden of these diseases is substantial, and government-funded research is unlikely to crowd out private investment. Second, infectious and parasitic diseases tend to cross borders. This suggests that the benefit of curing a disease is not limited to a single country, but rather reaches all countries to which the disease might spread.

rectangular at the disease-country-year level and disease-funder-year level. Thus, we have a sample of funders that ever funded one of the diseases between 2007 and 2014.

3.5.2 Disease burden

We use a standard measure of disease burden from the World Health Organization's (WHO) Global Burden of Disease project. The WHO reports the burden of disease in terms of DALYs lost, an estimate of years of life lost due to premature mortality and years of life lost due to time lived in less than full health. The WHO reports burdens by disease and country for the years 2000 and 2012. We linearly impute values between 2000 and 2012. As a robustness check, we also use country-year-disease mortality data from the Global Health Data Exchange's Global Burden of Disease Study.

We match the disease burden data to the funding data at the disease level. Some diseases in G-FINDER are not included in the disease burden data and vice versa, so our sample consists of 15 diseases.[8] Neither Ebola nor Zika are in our sample because the burden of disease datasets do not provide separate breakdowns for either one, and Ebola was only introduced in the G-FINDER data in the Policy Cures 2014 survey.[9]

3.5.3 State of science

Scientific knowledge about a disease is another potential determinant of research investment for the disease. Funders might devote more money to diseases with a more

[8] For example, rheumatic fever, included in the G-FINDER data, was not listed as a specific item in the Global Burden of Disease data and thus not included in our sample.

[9] Recent analysis by et al. Fitchett (2016) shows that funding for Ebola research increased substantially between 2014 and 2015, when the outbreak peaked. Though accounting for a very small share of total funding from 1997 to 2013, the European contribution for Ebola research exceeded American funding from 2014 to 2015 when American funding declined, consistent with the strategic responses we document in this paper.

advanced state of scientific knowledge, perhaps because such funding is more likely to lead to successful treatments. Furthermore, the existence of many published scientific papers reflects the interest and qualifications of academic researchers, who might submit more and better grant proposals.

We include a control variable for scientific knowledge which we measure as the number to date of publications about a disease indexed in the PubMed database. We include only publications that are coded in PubMed as journal articles, excluding letters, editorials, and reviews. Each article in PubMed includes keywords (or Medical Subject Headings) in its listing, which we use to assign to articles to diseases. Specifically, we use the "Entrez" tool from Biopython, an open-source package written in Python, to search the PubMed database for each disease and to extract information on all publications for which the disease is listed among the Medical Subject Headings. Our approach relies on the accuracy of the algorithm used by the National Library of Medicine to assign Medical Subject Headings.

As a robustness check, using data from IMS Health (now known as Quintiles IMS), we include a measure of recent drug innovation as an explanatory variable. We define recent innovation as the number of new treatments introduced for a disease since 1987. Diseases like HIV have experienced significant improvements in available treatments, whereas innovation in other diseases (such as malaria) has been less dramatic.

3.5.4 Congressional data

To construct our instrumental variables (as described in Section 3.4.1), we use data on the composition of the House and Senate appropriations committees (Stewart III and Woon, 2017), as well as data on research-intensive universities. In 2015 the Carnegie

Classification of Institutions of Higher Education classified 115 universities as classified as having the highest research activity (Center for Postsecondary Research, 2016). We count the university if it is in the state of the member of Congress, even if it is not in the member's district, because university alumni live throughout the state and support funding for the university (Chatterji et al., 2017).

3.5.5 Other country-level data

We also use country-level information on gross domestic product (GDP) per capita, downloaded from the World Development Indicators database. We adjust the amounts for purchasing power parity and inflation (2011 US dollars).

3.6 Results

3.6.1 Summary statistics

The sample includes 15 diseases: 6 infectious and 9 parasitic diseases for which we had data on both funding and disease burden. The data sample includes the period from 2007 to 2014 and 398 funders: 259 government agencies and 139 NGOs. The 41 countries include 6 in Africa, 8 in Asia, 2 in Australia, 17 in Europe, 3 in North America, and 5 in South America. For a given disease in a given year, a funder allocated a mean of \$200,000. Aggregating to a country level generates a mean of \$1.5 million (Table 3.3).

Diseases with a greater burden and more scientific knowledge tend to have greater funding outlays (consistent with Hypothesis 5). For example, HIV/AIDS has the greatest global disease burden, number of scientific publications to date, and global outlays (Table 3.1). The global outlays for HIV are predominately from government agencies (87% of funding) and the remainder from NGOs and foundations. For a typical disease, government agencies account for two thirds of funding.

Funding for neglected diseases by the US government is much higher than funding by other governments, both in absolute terms (Table 3.2) and relative to national income (Figure 3.1) (consistent with Hypotheses 6 and 7). The US government accounted for 59 percent of the total funding outlays for the 15 diseases in our sample, with the majority of that funding coming from the NIH (Table 3.2). Furthermore, measured as a share of national income, US funding for neglected diseases is at least triple that of any other country except the UK (Figure 3.1).

Funding outlays by other countries are not necessarily proportional to the number of scientific publications and burden of disease. For example, the government of Brazil provides less medical research funding for HIV/AIDS than for dengue, leishmaniasis, and malaria, each of which has a smaller burden of disease in Brazil than does HIV/AIDS (Table 3.1). One interpretation of the pattern is that Brazil may spend less on HIV/AIDS because it benefited from the funding for HIV/AIDS provided by the US. Indeed, the US heavily funded HIV/AIDS medical research, which allowed other countries to focus on other diseases of local importance. Hence, research on dengue received more outlays in Latin America and the Caribbean than did HIV/AIDS (consistent with Hypothesis 7).

3.6.2 Regression results

Recall that the dependent variable is the log of disease-funder-year outlays. Many of the independent variables are also in logs, so their coefficients are elasticities. In the tables with the regression results (beginning with Table 3.4), we include both the instrumental variable results and the ordinary least squares results. We present regression results for government agencies only (Table 3.4) and for both government agencies and private foundations combined (Table 3.5). There are 15 diseases, 8 years, and 398 funders, for a total of 47,760 observations. One year is lost due to lagged values when estimating the regressions, so in the regressions the number of observations is 41,790 (with all funders) or 27,195 (with only government agencies).

The first-stage of the regression results yields positive, statistically significant coefficients on the average number of research-intensive universities represented by Congressional appropriations committee members (Tables 3.4-3.7). The results suggest that a higher number of research-intensive universities represented on a Congressional appropriation committee yields higher research funding. This positive relationship between Congressional representation and outlays is also evident in Figure 3.2.

The sign on US government outlays differs between the ordinary least squares (OLS) and instrumental variable specifications (Table 3.4). Whereas the OLS results have a positive coefficient on US outlays, the instrumental variable specification gives the opposite result. The difference in sign suggests that unobserved factors drive R&D in both the US and other countries and create a spurious positive correlation in the OLS. Sargan test results indicate that the instrumental variables are uncorrelated with the residuals, and therefore are acceptable instruments. When the endogeneity of US outlays is accounted for, a 10 percent increase in US government outlays is associated with a decrease in outlays by funders in other countries in the following year (consistent with Hypothesis 6). The decrease ranges from 2 percent (Table 3.5) to 3 percent (Table 3.4).

Disease burden appears to influence outlays, consistent with Hypothesis 5. A 10 percent greater disease burden is associated with 1 percent greater outlays by the US government and by other governments. Likewise, outlays relate to scientific knowledge. A 10 percent greater number of scientific articles to date for a disease in a year is associated with a 10 percent increase in US government outlays. For government funders from other countries, the effect is half as large (Table 3.4). The coefficient on the HIV/AIDS indicator variable is positive and significant (Table 3.4). This is not surprising because HIV/AIDS receives more US funding than all other infectious and parasitic diseases combined (Table 3.1).

The sign on the coefficient for lagged GDP per capita is not statistically significant in most of the regression results. Because we include funder fixed effects, the coefficient on GDP per capita captures within-country variation over time. Normally, we would expect spending to increase when a country's economic performance is strong. The coefficient could plausibly be negative if outlays are intended as economic stimuli, but again, are typically not statistically or economically significant.

Table 3.6, shows the results when we interact the local disease burden with US outlays. The results suggest that funders with a large local disease burden are highly responsive to changes in US outlays for that disease, while funders with no local disease burden react little (the coefficient on US outlays alone was statistically and economically insignificant). In general, diseases with small local burdens receive less funding, so the potential for a negative response is limited.

We also examine the extensive margin; that is, whether other funders start or stop funding a disease in a given year in response to changes in US outlays for the disease in the previous year. The dependent variable for the analysis summarized in Table 3.7, was an indicator variable for whether outlays are positive. We observe a negative relationship between US outlays and subsequent starting or stopping of outlays by other funders for a given disease, but the effect is small. Countries are unlikely to start or stop funding for a disease entirely based on US medical research funding actions. Hence, the effects of US outlays seem to occur on the intensive margin (Table 3.6) rather than on the extensive margin (Table 3.7).

3.6.3 Results from robustness checks

We conduct five robustness checks (Appendix A). First, we include a count of the number of treatments introduced since 1987 to examine how the availability of existing treatments influence funding outlays. The availability of treatments is associated with higher levels of funding (Table 3.8). Perhaps these diseases receive more funding because there is a record of success in developing treatments for these diseases. Regardless of the reason for the positive relationship between the number of treatments and amount of funding, the results for the response to changes in US outlays are consistent with the results of the main analysis.

Second, rather than using the composition of Congressional appropriations committees as the instrumental variable, we use the NIH budget. We subtract from the budget the funding for the disease in question (although it is a small share of the total, we want to avoid having outlays for that disease on both the left and the right sides of the equation). The rationale for the validity of this instrument is the same as that for the composition of the Congressional appropriations committees; that is, disease funding in the US is correlated with the total NIH budget, but the total NIH budget should not affect the decisions of other funders directly. In this specification, the coefficient on US outlays is -0.2 (Table 3.9), which is comparable to results of the main analysis.

Third, we drop the scientific knowledge control variable, because our measure (number of scientific publications to date) might be simultaneously determined by funding. With this omission, the US outlays coefficient was slightly smaller but qualitatively similar: -0.26 with the scientific knowledge control variable compared to -0.18 without it (Table 3.10).

Fourth, we incorporate an alternative measure of disease burden. Recall that DALYs are available from only 2000 and 2012, and we linearly interpolate DALY values for the other years. Annual mortality data are available. The results are largely unchanged (Table 3.11) when using mortality rather than DALYs as a measure of disease burden.

Finally, we replace the 1-year lag for US outlays with a 2-year lag, in case it takes more time for non-US funders to observe a change in US outlays and implement a response. With a longer lag, the coefficient on US outlays was smaller in magnitude than that of the 1-year lag and not statistically significant (Table 3.12).

3.6.4 Discussion

What is the economic magnitude of the strategic response by non-US funders to American investment in medical research? Based on the US share of outlays (about one half) and the estimated elasticities from the regressions (-0.2 to -0.3), our results suggest that if the US increases outlays by one dollar for a disease, then the net outlay will be around \$0.70 to \$0.80.

Regardless of the explanation for the response – i.e. whether free riding, crowding out, or optimal reallocation by non-US funders – this result has implications for estimating the impact of US funding. Demonstrating that basic research has positive, measurable effects is important for sustaining government funding. Indeed, the NIH website emphasizes its impact on health, society, and the scientific community.[10] A large literature in economics estimates the effect of NIH funding on the production of scientific papers and development of new drugs. In general, if the response of non-US funders is ignored, then the funding is measured incorrectly. This is likely to bias downward estimates of NIH impact.

3.7 Conclusions

Governments and foundations advance science by funding research and then sharing the results with the public. Funding of medical research may exhibit free riding or crowding out, particularly among the high-income countries that are capable of financing it. In our sample, the US government provides more than half of global government and foundation funding for research on infectious and parasitic diseases (Table 3.2). Also, US medical research spending as a share of GDP is triple that of all other high-income countries except the UK (Figure 3.1). In 2003, the Commissioner of the US Food & Drug Administration noted the disparity in medical research funding between the US and other high-income countries as well as its implications:

"Our governments need to start by sharing the burden of the increasingly complex basic science that goes into the development of new drugs and biologics. In the United States, we've responded to the new opportunities that exist in the lab, by doubling our NIH budget to over $27 billion. As a share of GDP, this is about four times as much as European Union countries spend. But on an interconnected planet, all of this spending turns into biomedical knowledge that is transmitted worldwide for the good of public health worldwide. If other developed countries contributed to this worldwide effort in

[10] For example, see `https://www.nih.gov/about-nih/what-we-do/impact-nih-research`

proportion to their GDP, we would build the foundations for better treatments much faster" (McClellan, 2003).

We document how governments respond to other funders in supporting medical research. First, we show a negative correlation between outlays for a disease by the US government and outlays by other governments, NGOs, and foundations in the following year, while accounting for the endogeneity of US outlays. We also find that in Latin America and the Caribbean, HIV/AIDS imposed the greatest disease burden, but received less in total funding outlays than diseases like Chagas and dengue. Indeed, the government of Brazil spent less on HIV/AIDS research than on Chagas and dengue research, even though Brazil's disease burden from HIV/AIDS was 100 times greater than the burden from Chagas and dengue (Table 3.1). A typical model of funding allocation that ignores the role of a dominant funder like the NIH would have difficulty explaining these patterns.

We focus on infectious and parasitic diseases in this paper, in part because of the availability of detailed data. However, our results might hold for other diseases. In 2014, the NIH budget for all diseases was more than 12 times greater than its UK equivalent, the Medical Research Council.[11] This ratio is similar to that observed for our subset of diseases (Table 3.2). In future research, it would be interesting to examine whether the results change if we examine a disease that burdens rich and poor alike, such as cancer or diabetes.

We find a negative relationship in outlays across funders, but the magnitude is less than one, meaning that other governments reduce outlays by less than one dollar when

[11] The US NIH budget in fiscal years 2014 and 2015 was approximately $30 billion while the UK MRC budget in 2014-15 was less than £1 billion.

the US increases outlays by one dollar. This finding is consistent with our model, which predicts that the relationship will be less than one-to-one when there are differences in budgets across funders. Furthermore, funders may have other objectives that we do not consider explicitly, including a desire to fund research at favored institutions (Hegde and Mowery, 2008; Hegde, 2009) or to show progress fighting a disease. Also, there might be other frictions that mute awareness or action on funding changes.

If we assume that all high-income countries have similar research productivity and assessments of the value of curing diseases, we should expect roughly similar per-capita spending across countries. However, the US government provides more than half of global government and foundation funding for research on the 15 infectious and parasitic diseases in our analysis. Furthermore, US medical research spending as a share of GDP is triple all other high-income countries, other than the UK. This evidence is consistent with free riding. While much of our evidence is consistent with free riding, the regression results are also consistent with optimal reallocation. Indeed, according to a program officer of the Burroughs Wellcome Fund, "We avoid funding areas that the federal government is funding in order to focus on the underserved. This is how many of our philanthropic peers operate. For example, when the NIH developed its translational science programs, we retired ours." Likewise, asked about the objectives of the Gates Foundation, an employee wrote, "the primary driver is perceived neglect and opportunity for impact in a disease area which brings together both health impact and other donor support." [12] The Congressionally Directed Medical Research Programs Review Process in the US is tasked with identifying and avoiding duplicative research funding, but fo-

[12] Sources: email correspondence with a Gates Foundation employee on August 8, 2012 and with a Burroughs Wellcome program officer on December 9, 2016.

cuses primarily on avoiding overlap across US government agencies and with NGOs; in fact, a recent evaluation of this process makes no mention of non-US funding (National Academies of Sciences, Engineering, and Medicine, 2016).

Without a general equilibrium analysis, we cannot determine the extent to which our results indicate free riding or optimal reallocation. Nevertheless, it is useful to be aware of how global resources shift when the US changes its medical research funding outlays.

Documenting government responses to changes in medical research funding outlays is relevant to both research and policy sectors. Scholars should be aware that estimates of the impact of one additional dollar of NIH funding could underestimate the effect, because the net increase in funding for that disease will be smaller.

Policy makers should be aware of how governments adjust funding and consider enhancing international coordination, regardless of whether the negative relationship across funders is socially optimal. The evidence in this paper suggests that governments should increase efforts to coordinate on medical R&D funding through organizations such as the World Health Organization as they do in other areas, including military defense and environmental regulation.

Table 3.1: Summary Statistics: Diseases

Indication	Count of Govt. Agencies	Number of Publications to date (MM)	Global Disease Burden (000)	Global Mean Outlay ($MM)	USA Government Disease Burden (000)	USA Government Mean Outlay ($MM)	Brazil Gov. Disease Burden (000)	Brazil Gov. Mean Outlay ($MM)
Infectious Disease								
Dengue	63	6	1007	83	0	53	4	7
HIV/AIDS	97	74	101632	1124	494	840	838	0.8
Leprosy	17	11	219	10	0	5	1	1
Meningitis	29	7	41693	41	2	8	118	0.5
Trachoma	6	11	433	5	0	4	62	0
Tuberculosis	121	72	60296	410	32	180	326	1
Parasitic Disease								
Chagas disease	37	8	571	18	0	12	3	1
Hookworm disease	5	1	3469	9	0	2	15	0
Leishmaniasis	57	13	4986	48	0	22	37	2
Lymphatic filariasis	15	9	2534	13	0	5	17	0
Malaria	121	36	78236	458	46	174	130	2
Onchocerciasis	4	2	590	7	0	2	2	0
Schistosomiasis	19	12	3137	23	0	15	181	1
Trichuriasis	2	1	696	1	0	0.5	0.4	0
Trypanosomiasis	26	3	3741	41	1	16	11	0

Note: The disease burden is measured in disability-adjusted life years (DALYs) lost. *Source*: Authors' analysis using data from Policy Cures and the World Health Organization.

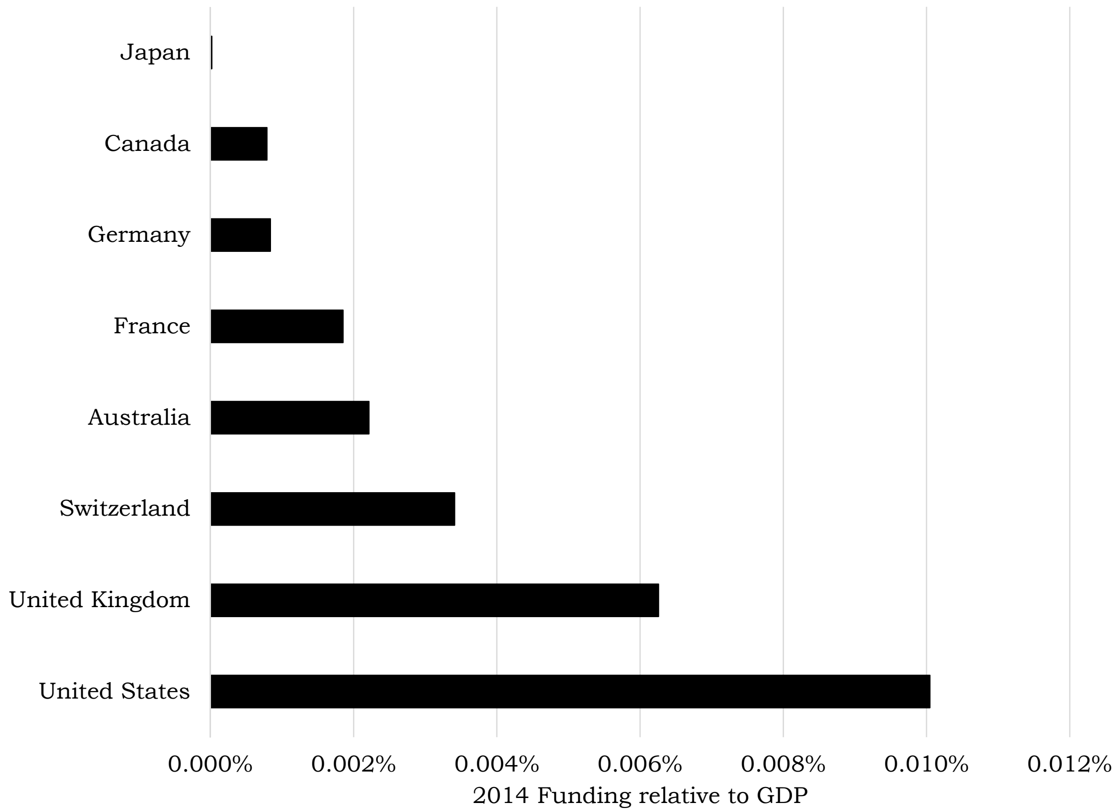


FIGURE 3.1: Percentage of national income for medical research on 15 infectious and parasitic diseases.

Source: Authors' analysis using data from Policy Cures and the World Bank.

Table 3.2: Summary Statistics: Funders

Funder	Percent	Total Outlays ($MM, 2007-2014) Infectious	Parasitic
Aggregated Government			
United States	58.63	8752	1989
United Kingdom	4.72	891	502
France	2.86	557	286
India	1.16	110	102
Australia	1.14	80	130
Germany	1.06	130	64
Canada	0.76	137	1
Netherlands	0.67	99	25
Brazil	0.57	63	41
Sweden	0.48	65	23
31 other governments	0.11	16	5
Government Agencies			
National Institutes of Health, USA	50.32	7572	1645
Agency for International Development, USA	3.89	642	70
Department of Defense, USA	3.46	406	227
Department for International Development, UK	2.27	296	120
Medical Research Council, UK	2.25	216	196
Institut Pasteur, France	1.07	102	94
National Health and Medical Research Council, Australia	0.93	61	110
Inserm - Institute of Infectious Diseases, France	0.83	107	45
Council of Medical Research, India	0.75	68	69
Centers for Disease Control and Prevention, USA	0.65	91	29
249 other government agencies	0.03	4	1
Non-Governmental Organizations			
Bill & Melinda Gates Foundation, USA	20.41	2257	1482
The Wellcome Trust, UK	3.52	273	372
UBS Optimus Foundation, Switzerland	0.06	7	4
Fundacio La Caixa, Spain	0.06	7	4
Starr Foundation, USA	0.06	11	0
Global Alliance for Vaccines and Immunizations, Switzerland	0.05	8	0
ExxonMobil Foundation, USA	0.04	1	7
amfAR, The Foundation for AIDS Research, USA	0.03	6	0
Global Fund to Fight AIDS, TB and Malaria, Switzerland	0.03	4	2
OPEC Foundation for International Development, Austria	0.03	5	0
129 other non-governmental organizations	0.003	0.3	0.2

Source: Authors' analysis using data from Policy Cures.

Table 3.3: Summary Statistics: Units of Observation

Unit of Observation (observations)	**Variable**	**Mean**	**Std Dev**
Disease, Funder, Year (47760)	Annual outlay by a funder ($MM)	0.2	3
	Local disease burden (000)	166	1093
	Local disease burden, deaths (000)	3	28
Country, Year (328)	GDP per capita ($)	29764	22768
Disease, Year (120)	Annual US outlays ($MM)	88	211
	Number of publications to date (MM)	18	23
	Disease burden in poor countries (000)	12862	21043
	Disease burden in poor countries, deaths (000)	233	414
	Number of treatments launched since 1987	2	5
Year (8)	Lag research universities per Congressional appropriations member	3.7	0.1
	NIH budget ($BN)	30	617

Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.4: Strategic funding decision. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.095		-0.264
	(0.013)		(0.080)
Log local disease burden	0.038	0.110	0.076
	(0.037)	(0.008)	(0.038)
Log burden in poor countries	0.116	0.155	0.171
	(0.019)	(0.002)	(0.021)
Infectious except HIV indicator	0.002	-0.560	-0.202
	(0.052)	(0.003)	(0.068)
HIV indicator	-0.076	1.591	0.494
	(0.198)	(0.011)	(0.232)
Log number of publications to date	0.281	1.100	0.679
	(0.037)	(0.004)	(0.097)
Lag log GDP per capita	-0.549	1.017	-0.228
	(0.166)	(0.046)	(0.155)
Lag research universities per Congressional appropriations member		2.561	
		(0.029)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.5: Strategic funding decision. Government funders and private funders.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.072		-0.189
	(0.010)		(0.058)
Log local burden	0.060	0.142	0.096
	(0.031)	(0.008)	(0.032)
Log burden in poor countries	0.087	0.147	0.125
	(0.015)	(0.002)	(0.016)
Infectious except HIV indicator	0.008	-0.556	-0.139
	(0.043)	(0.003)	(0.056)
HIV indicator	-0.055	1.503	0.335
	(0.157)	(0.016)	(0.180)
Log number of publications to date	0.220	1.087	0.506
	(0.027)	(0.004)	(0.070)
Lag log GDP per capita	-0.469	1.048	-0.257
	(0.145)	(0.046)	(0.134)
Lag research universities per Congressional appropriations member		2.612	
		(0.022)	
Funder fixed effect	Yes	Yes	Yes
Observations	41790	41790	41790

Standard errors in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.6: Strategic funding decision with interaction term between US outlay and local disease burden. Government funders only.

		Instrumental Variables		
	OLS	First Stage 1	First Stage 2	Second Stage
Lag log annual US outlays	0.087			0.055
	(0.017)			(0.057)
Log local disease burden	-0.132	1.788	14.695	6.325
	(0.245)	(0.101)	(0.170)	(1.674)
Log local disease burden x Lag log annual US outlays	0.010			-0.351
	(0.015)			(0.094)
Log burden in poor countries	0.115	0.154	0.191	0.188
	(0.019)	(0.002)	(0.032)	(0.025)
Infectious except HIV indicator	0.007	-0.562	-0.947	-0.357
	(0.053)	(0.003)	(0.075)	(0.096)
HIV indicator	-0.144	1.589	8.377	2.928
	(0.254)	(0.011)	(0.425)	(0.783)
Log number of publications to date	0.277	1.099	1.189	0.745
	(0.037)	(0.004)	(0.118)	(0.110)
Lag log GDP per capita	-0.564	1.111	2.206	0.285
	(0.169)	(0.047)	(0.155)	(0.229)
Lag research universities per Congressional appropriations member		3.126	1.252	
		(0.034)	(0.099)	
Log local burden x Lag research universities per		-0.450	0.856	
Congressional appropriations member		(0.025)	(0.040)	
Agency fixed effect	Yes	Yes	Yes	Yes
Observations	27195	27195	27195	27195

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.7: Strategic funding decision at extensive margin. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.007		-0.023
	(0.001)		(0.007)
Log local disease burden	0.003	0.110	0.006
	(0.003)	(0.008)	(0.003)
Log burden in poor countries	0.009	0.155	0.013
	(0.001)	(0.002)	(0.002)
Infectious except HIV indicator	-0.000	-0.560	-0.018
	(0.004)	(0.003)	(0.006)
HIV indicator	-0.014	1.591	0.034
	(0.014)	(0.011)	(0.018)
Log number of publications to date	0.021	1.100	0.056
	(0.003)	(0.004)	(0.008)
Lag log GDP per capita	-0.044	1.017	-0.016
	(0.014)	(0.046)	(0.013)
Lag research universities per Congressional appropriations member		2.561	
		(0.029)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.8: Strategic funding decision after controlling the number of existing treatments. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.089		-0.369
	(0.012)		(0.142)
Log local disease burden	0.013	0.081	0.050
	(0.039)	(0.007)	(0.040)
Log burden in poor countries	0.111	0.147	0.177
	(0.019)	(0.001)	(0.029)
Infectious except HIV indicator	0.125	-0.417	-0.071
	(0.048)	(0.003)	(0.074)
HIV indicator	-1.268	0.227	-1.162
	(0.358)	(0.009)	(0.357)
Log number of publications to date	0.209	1.012	0.678
	(0.033)	(0.003)	(0.146)
Lag log GDP per capita	-0.571	0.986	-0.175
	(0.166)	(0.045)	(0.210)
Number of treatments launched since 1987	0.085	0.128	0.108
	(0.021)	(0.001)	(0.025)
Lag research universities per Congressional appropriations member		2.568	
		(0.028)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.9: Strategic funding decision using the NIH budget as IV. Government funders only.

	OLS	Instrumental Variables	
		First Stage	Second Stage
Lag log annual US outlays	0.095		-0.179
	(0.013)		(0.064)
Log local disease burden	0.038	0.110	0.067
	(0.037)	(0.008)	(0.038)
Log burden in poor countries	0.116	0.155	0.158
	(0.019)	(0.001)	(0.021)
Infectious except HIV indicator	0.002	-0.559	-0.153
	(0.052)	(0.003)	(0.062)
HIV indicator	-0.076	1.590	0.358
	(0.198)	(0.011)	(0.222)
Log number of publications to date	0.281	1.098	0.584
	(0.037)	(0.004)	(0.081)
Lag log GDP per capita	-0.549	0.530	-0.304
	(0.166)	(0.031)	(0.167)
Lag log NIH budget		12.666	
		(0.085)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.10: Strategic funding decision without number scientific publications. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.149		-0.182
	(0.017)		(0.070)
Log local burden	0.076	0.333	0.187
	(0.037)	(0.028)	(0.044)
Log burden in poor countries	0.153	0.378	0.277
	(0.021)	(0.006)	(0.032)
Infectious except HIV indicator	0.212	0.332	0.321
	(0.053)	(0.011)	(0.058)
HIV indicator	-0.057	2.118	0.644
	(0.197)	(0.048)	(0.241)
Lag log GDP per capita	-0.504	1.504	-0.051
	(0.166)	(0.061)	(0.159)
Lag research universities per Congressional appropriations member		2.955	
		(0.043)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.11: Strategic funding decision with alternative disease burden measure. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
Lag log annual US outlays	0.049		-0.237
	(0.009)		(0.074)
Log local disease burden, deaths	0.095	-0.067	0.076
	(0.036)	(0.005)	(0.036)
Log burden in poor countries, deaths	0.036	0.248	0.106
	(0.015)	(0.001)	(0.022)
Infectious except HIV indicator	-0.240	-0.447	-0.370
	(0.076)	(0.008)	(0.083)
HIV indicator	0.060	1.916	0.604
	(0.220)	(0.012)	(0.250)
Log number of publications to date	0.278	0.606	0.454
	(0.036)	(0.001)	(0.056)
Lag log GDP per capita	-0.483	1.262	-0.160
	(0.163)	(0.052)	(0.156)
Lag research universities per Congressional appropriations member		2.749	
		(0.035)	
Agency fixed effect	Yes	Yes	Yes
Observations	27195	27195	27195

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

Table 3.12: Strategic funding decision with 2-year lagged US government outlay. Government funders only.

		Instrumental Variables	
	OLS	First Stage	Second Stage
2-year-lag log annual US outlays	0.094		-0.062
	(0.013)		(0.077)
Log local burden	0.027	0.109	0.044
	(0.036)	(0.009)	(0.037)
Log burden in poor countries	0.109	0.129	0.129
	(0.019)	(0.002)	(0.023)
Infectious except HIV indicator	-0.011	-0.639	-0.112
	(0.053)	(0.003)	(0.067)
HIV indicator	-0.072	1.669	0.188
	(0.197)	(0.012)	(0.231)
Log number of publications to date	0.295	1.143	0.475
	(0.038)	(0.005)	(0.092)
Lag log GDP per capita	-0.870	-0.056	-0.723
	(0.207)	(0.110)	(0.224)
Lag research universities per Congressional appropriations member		2.553	
		(0.057)	
Agency fixed effect	Yes	Yes	Yes
Observations	23310	23310	23310

Standard errors are in parentheses and are clustered at the agency level.
Source: Authors' analysis using data from Policy Cures, PubMed, the World Bank, and the World Health Organization.

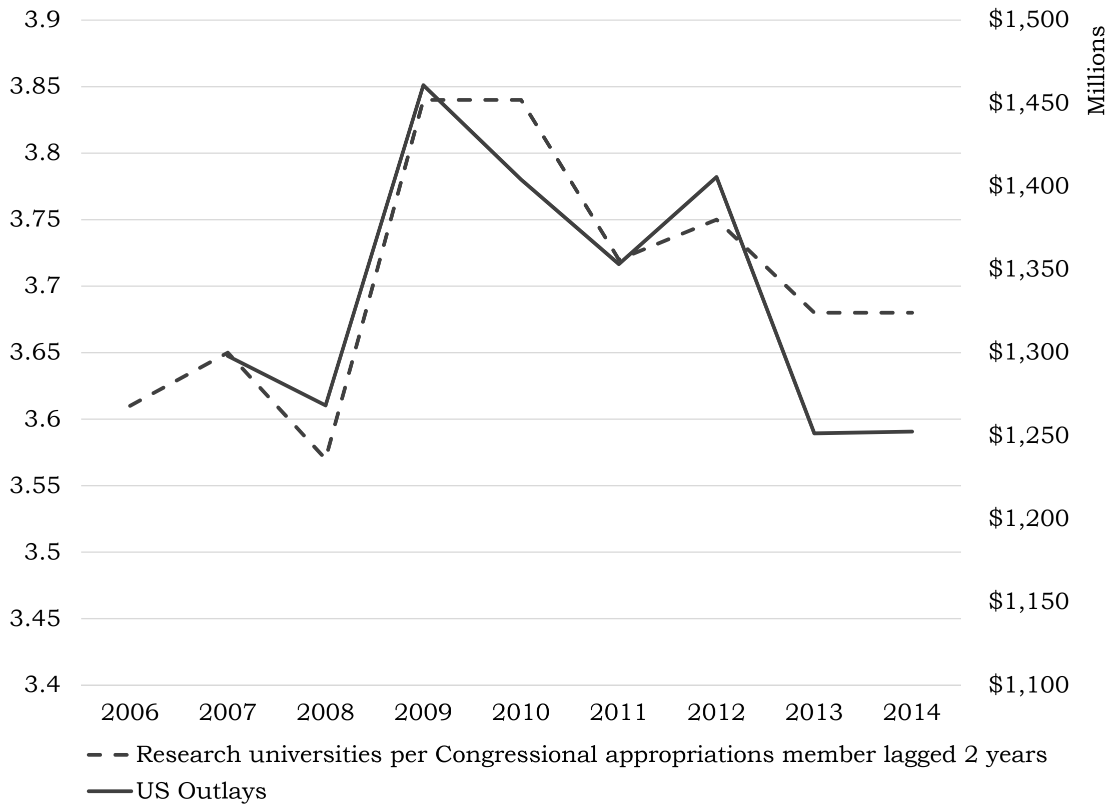


FIGURE 3.2: The magnitude of US outlays appears to depend in part on representation of research-intensive universities on US Congressional appropriations committees.

Source: Authors' analysis using US Congressional data, Carnegie university classifications, and Policy Cures data.

4

Who Cares? Corporate Social Responsibility in Drug Development

4.1 Introduction

Companies are increasingly engaging in corporate social initiatives, but we know little about why one company in a given industry engages and another would not. We examine connectedness to the customers, as well as related experience which affects capabilities. Understanding these differences can help us identify drivers of corporate strategy and how policy can influence them.

We measure corporate social initiatives as drug development for infectious and parasitic diseases endemic in developing countries. These neglected diseases cause suffering in more than one hundred countries and affect more than one billion people. Developing a new treatment for dengue, a disease known as "breakbone fever" which currently has no specific treatment, could relieve the suffering of millions of people.[1] Unlike "green-

[1] Information on the burden of neglected diseases such as dengue is available from the World Health

washing” in which companies make symbolic gestures (Chatterji et al., 2009), drug development for neglected diseases is costly (DiMasi et al., 2016), unlikely to be directly profitable (Trouiller et al., 2002), and socially impactful (Kremer, 2002).

We find that a company conducts more trials for a given neglected disease if its headquarters is in a country with former colonies in which the disease is endemic. In Belgium, Britain, and France, for example, scientists and other employees have family and friends living in former colonies or who immigrated from former colonies. Also, employees hear news stories about former colonies and travel to former colonies for business and pleasure. For them, the neglected diseases are not abstract but real.

The chief scientific officer of Janssen, a company founded in Belgium, began his career as a physician focusing on infectious disease research in Congo, a former colony of Belgium. He later championed the development of bedaquiline, a drug for tuberculosis – a disease endemic in Congo. Bedaquiline is the first drug for pulmonary multi-drug resistant tuberculosis with a novel mechanism of action in more than 40 years.

Likewise, Andrew Witty, the chief executive officer of Britain’s GlaxoSmithKline (GSK) is a British citizen from 2008 to 2017 started his career as managing director in South Africa, a former British colony. He later championed development of drugs and vaccines for neglected diseases. “If you’re in South Africa,” he said, “you have to address the challenges the society tries to address” (Dentzer, 2009). He added, “I want GSK to be a very successful company, but not by leaving the population of Africa behind” (McNeil, 2010).

People working for drug companies need reasons to be proud of their companies,

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Organization neglected tropical disease fact sheets at `http://www.who.int/neglected_diseases/mediacentre/factsheet/en/`.

given public scrutiny of drug company prices and profit. Employees need a story to tell their family members and themselves about the good deeds done by the company. Because employees value purpose and meaningfulness at work (Burbano, 2016), social investment can help companies reduce costs or boost employee productivity (Flammer, 2015a; Flammer and Luo, 2017; Shan et al., 2016). Scientists appear to be motivated in part by non-pecuniary rewards (Stern, 2004). According to GSK executive Witty, efforts to help people in developing countries "will be very positively received by our employees... because they want to be part of trying to solve these issues" (Dentzer, 2009).

Executives can also boast to shareholders and regulators of their efforts to treat neglected diseases. In its 2016 annual report, GSK executives boasted that phase III clinical trials of its malaria vaccine had been successful and that the vaccine would be available in sub-Saharan Africa in 2018. Often shareholders want to encourage social investment and thus structure executive compensation to encourage it (Hong et al., 2016). Social investments can boost company performance (Freeman, 1984; Jones, 1995; Surroca et al., 2010; Cheng et al., 2014; Ioannou and Serafeim, 2015; Madsen and Rodgers, 2015), including giving companies easier access to financial markets (Cheng et al., 2014) and can cushion share price drops from bad news (Shiu and Yang, 2017). Companies also make social investments to alleviate regulatory pressure (Werner, 2015). The extent to which regulators and other external constituents influence social investments depends on with whom they interact at the company (Delmas and Toffel, 2008). However, we cannot rule out the possibility that social investments driven by the executive are inefficient or unfair to shareholders (Friedman, 1970; Baron, 2007).

We do not believe that consumer demand is an important factor in drug industry social investment. In other settings, corporate social investment affects profit through consumer preferences (Siegel and Vitaliano, 2007; Baron, 2008; Flammer, 2015b). However, few consumers of GSK's asthma drugs are aware that GSK is developing a malaria vaccine for sub-Saharan Africa.

This is the first study to show the influence of historic colonial ties on modern corporate social initiatives. The study contributes to a literature on the importance of business location. For example, Fabrizio and Thomas (2012) showed that even though the drug market is global, demand in the country of headquarters drives drug development. For example, between 1980 and 2001, British and U.S. firms developed five of the six new antimigraine products. Migraines are disproportionately suffered by women, and doctors and patients take the disease more seriously than those in other countries, such as Japan.

Also, studies show that colonial ties leave a lasting mark. For example, countries that were inhospitable to settlement tended to have colonizers that extracted resources rather than building up institutions, and those countries have lower GDP per capita today (Acemoglu et al., 2001).

Other studies also highlighted the importance of location matters for business strategy. Companies are more willing to invest in countries with greater policy risk if the company headquarters is located in a country with greater policy risk (Holburn and Zelner, 2010). Furthermore, companies are more likely to commercialize their products in countries with which they share a border or language (Kyle, 2006). The local environment affects the focus of innovative companies (Fabrizio and Thomas, 2012), their organizational structure (Furman, 2003), their internal linkages for knowledge flow (Alcácer and Zhao, 2012), and their success (Porter and Stern, 2001).

Only recently have studies demonstrated the importance of location for corporate social responsibility. Husted et al. (2016) showed that headquarters location matters because of what other firms are doing near the corporate headquarters. However, we show that it is not only the geographic proximity of other companies, but the cultural ties of other countries that matter.

We also find that companies invest more in social initiatives if they have related expertise. For example, GSK and Merck developed drugs for commercially profitable infectious diseases, and extended their work to infectious diseases endemic in developing countries. Both GSK and Merck had previously developed drugs for HIV, and Merck had developed a drug for Hepatitis C, and later both companies conducted clinical trials for another infectious disease: dengue. Hence, companies focus on the societal problems that they are best equipped to help solve, as advocated by Porter and Kramer (2006). These results are consistent with previous studies showing that firms need the capability to do the work (Cohen and Levinthal, 1990; Fabrizio, 2009) and that managers tend to identify new opportunities adjacent to existing opportunities (Rosenkopf and Nerkar, 2001).

We do not find that companies unengaged in drug development for diseases of poverty compensate by lowering prices in poor countries for drugs for other diseases, such as diabetes and heart disease. Indeed, we find a positive relationship between companies engaged in corporate social initiatives through drug development and companies applying equitable pricing to drugs across their portfolio. For example, Britain's GSK is second-highest in clinical trials for neglected diseases, with nearly one trial started per year, and rated highest on equitable pricing. GSK's equitable pricing covered "a broad range of diseases, including HIV/AIDS, lower respiratory infections, asthma, pertussis and hypertensive heart disease" (Access to Medicine Foundation, 2016).

4.1.1 Background on neglected diseases

We measure corporate social responsibility as drug development for diseases of poverty, also known as neglected diseases. Neglected diseases are either infectious or parasitic, cause enormous loss measured in disability-adjusted life years lost, have few available treatments, and have little profit potential. There is little incentive to develop drugs for neglected diseases, even with the expansion of intellectual property protection in developing countries (Kyle and McGahan, 2012), because most of the people suffering from the diseases are poor. A commitment of more than $3 billion would be needed to create the same incentive for developing a treatment for a neglected disease as for a commercial disease, according to Berndt et al. (2007).

We define neglected diseases based on the seminal paper by Trouiller et al. (2002) who wrote, "We examined specifically registration of new chemical entities for tropical diseases (defined here as parasitic diseases [malaria, African trypanosomiasis, Chagas' disease, schistosomiasis, leishmaniasis, lymphatic filariasis, onchocerciasis, intestinal nematode infections], leprosy, dengue, Japanese encephalitis, trachoma, and infectious diarrhoeal diseases) and tuberculosis. These infectious diseases represent a substantial burden among developing countries, and together account for 11.4% of the global disease burden. We find that only 1% of the 1393 new chemical entities marketed between 1975 and 1999 were registered for these diseases."

Developing drugs and charging low prices in order to eradicate a disease is surely not directly profitable. In its 2015 Corporate Social Responsibility Report, the Sanofi CEO wrote of his goal to eradicate African trypanosomiasis, also known as "sleeping sickness." "The expertise we have developed along the way has had a profound effect, particularly in the developing world... over the last decade, sleeping sickness treatments have saved more than 180,000 lives, and we are on the way to eliminating the disease by 2020."[2]

4.1.2 Background on pharmaceutical R&D

Pharmaceutical R&D consists of drug discovery and development. In drug discovery, a targeted chemical or biological molecule is identified and isolated. In drug development, the targeted molecule is first tested in preclinical trials in animals. If the results suggest that the product is safe and effective, then it will be tested in humans in clinical trials. A phase I clinical trial involves testing the product in multiple dosage forms on a small number of healthy volunteers in order to generate preliminary therapeutic evidence of efficacy and toxicity. A phase II clinical trial involves more patients and further evidence of efficacy. If the results are still promising, then the product enters phase III clinical testing. A phase III clinical trial can include tens of thousands of patients in a double-blind experimental design. If the trial results are positive, the drug sponsor applies for regulatory approval. Our analysis includes clinical trials in phases I through III.

Pharmaceutical R&D is risky and costly, unlike "greenwashing" in which companies make merely symbolic efforts (Chatterji et al., 2009). For major drug manufacturers, the average economic cost of successfully bringing a new commercial drug to market is \$2.6 billion (DiMasi et al., 2016) which includes both the opportunity cost of capital and the low success rate of only about 12% of molecules tested in humans reaching the market (DiMasi et al., 2016).

[2] The 2015 Corporate Social Responsibility Report for Sanofi is available at `http://en.sanofi.com/Images/47679_CSR_Report_2015_EN.pdf`.

4.2 Theory

A model highlights our assumptions and predictions. Consider a corporate executive who chooses investment in product development and then price. Higher levels of investment are costly, but increase revenue and consumer surplus.

$$u(p, x) = R(p, x) + \alpha S(p, x) - C(x, x_i, \kappa)$$

where R is the revenue which depends on the price p and the investment x. The second term S is the consumer surplus which the executive cares about, though perhaps less than the consumer, so $0 \leqslant \alpha \leqslant 1$. We can think of α as being the connectedness of the corporate decision maker to the consumer. In the empirical model, we will estimate α based on the ties of the country of headquarters to the people in developing countries who benefit from the product. The third term is cost C which depends on the investment in the product and the investment in other products i with spillovers, as well as public knowledge of product development κ.[3]

We assume that revenue, consumer surplus, and cost are increasing in the investment. The cost of the investment is decreasing in the investment in other products (due to spillovers) and in the public knowledge. The firm's manager maximizes utility by first choosing investment x and then price p.

In the appendix (section C), we solve for a simple version in which demand is linear and investment cost is quadratic. We work backward, solving price p and then solving

[3] The model includes only one product, taking investment in the firm's other product as given. In a model with multiple products, the level of investment would be higher to account for positive spillovers. Also, a model with multiple products would show multiple prices which is consistent with our estimation results in which companies are lowering prices across their portfolio of products, not just the products for neglected diseases. However, the simple one-product model is sufficient for providing intuition and four testable hypotheses.

x^*. We can show:

$$\delta x^* / \delta \alpha > 0 \tag{4.1}$$

$$\delta x^* / \delta x_i > 0 \tag{4.2}$$

$$\delta x^* / \delta \kappa > 0 \tag{4.3}$$

$$\delta p^* / \delta \alpha < 0 \tag{4.4}$$

The theory informs four hypotheses. Hypothesis 8 follows from equation 4.1. A company with a connection to the suffering from the disease will have decision makers who care more about alleviating the suffering (a higher α) and thus will invest more in development.

Hypothesis 8. *A company will invest more in social initiatives if the need is high in the former colonies of its country of headquarters.*

Whereas Hypothesis 8 concerns connections on the demand side, Hypothesis 9 concerns connections on the supply side. From equation 4.2, if a company is engaged in drug development for related diseases, then the development cost will tend to be lower. For example, if the company has experience with one infectious diseases, such as Hepatitis C, then it will be more aware of and have lower cost of developing drugs for another infectious disease, such as dengue.

Hypothesis 9. *A company will invest more in social initiatives if it has experience with related products (both profitable and unprofitable).*

Whereas Hypothesis 9 concerns the company's own experience with a class of diseases, Hypothesis 10 concerns society's shared knowledge of a disease. Investment will depend not only on the company's own experience, but also general knowledge of the product in society. If general knowledge of the basic science of the product is more advanced, then a company conducts more product development.

Hypothesis 10. *A company will invest more in a social initiative if the potential for impact is greater due to the state of science.*

Finally, connectedness will not only affect investment (Hypothesis 8) but also price. Hypothesis 11 (based on equation 4.4) concerns the price of the product as a function of the connectedness of the firm to the people in need.

Hypothesis 11. *A company will choose a lower price if it has connections to the need for the drug in developing countries.*

We test the hypotheses using the data described below.

4.3 Data

We use six data sources. First, we use pharmaceutical clinical trial data from the IMS LifeCycle R&D Focus data base. Second, we use country-level burden of disease data from the World Health Organization (WHO) global burden of disease data base. Third, we use data on former colonies from the GeoDist data base from CEPII. Fourth, we use disease-specific scientific publication data from PubMed. Fifth, we use firm financial data from Compustat. Sixth, we use company rankings from the Access to Medicine Foundation. We provide greater detail about each of these data sets below.

4.3.1 Clinical trials

We measure corporate social initiatives as clinical trials for neglected diseases using data from IMS Health. An observation in the IMS LifeCycle R&D Focus database includes the product name, therapeutic class, developer, and timing of each phase of clinical development from 1989 to the present. We use the number of clinical trials for each infectious and parasitic disease for a given firm in a given year. For a clinical trial with multiple companies in an alliance, we count the observation for each of the firms in the alliance.

4.3.2 Burden of disease

We use burden of disease which we measure as disability adjusted life years (DALYs) lost for each disease in each country as they appear in the WHO global burden of disease data base.[4] To measure the potential for social good, we use the burden of disease in low-income countries, i.e., former colonies of rich countries. To measure the commercial potential, we use the burden of disease in high-income countries.

4.3.3 Colony-colonizer relationship

We use data on former colonies in order to examine whether social initiatives depend on the burden of disease in former colonies of the country of headquarters. We match the colonial relationship between countries based on the Geodist database from CEPII. The Geodist database incorporates country-specific colonial links for 225 countries in the world, for which it identifies up to 4 long-term and up to 3 short-term colonizers in the history of the country. For each colonizer, we construct the burden of disease in its past

[4] http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html

colonies for each disease by aggregating the burden of that disease over past colonies.

4.3.4 State of science

We use data on the state of science to investigate how it affects clinical trials. We measure the state of science as the cumulative basic scientific articles indexed in the PubMed database. Each article in PubMed includes keywords (or medical subject headings) in its listing, which we use to assign to diseases. We include only publications that were coded in PubMed as journal articles, excluding letters, editorials, and reviews. We focus on basic science by excluding publications that mention a clinical trial in the medical subject header. We exclude articles about clinical trials because we already measure clinical trials in the IMS R&D Focus data.

4.3.5 Company financial data

We use firm financial information from the Compustat Capital IQ data base. We use data on profit, revenue, assets, and company headquarters location.

4.3.6 Company ratings

We measure company engagement in global health beyond clinical trials using the 2016 Access to Medicine Foundation report. The report includes an assessment of the equitable pricing policies and practices of 20 of the world's largest research-based (non-generic) pharmaceutical companies. The report assesses equitable pricing of medicines for people living in low- and middle-income countries. Companies receive a higher score if they use differential pricing based on socioeconomic factors between countries and within countries. According to the report, the diseases with the most equitably-priced products are: heart disease, lower respiratory infections (such as pneumonia), HIV/AIDS, diabetes, liver cirrhosis, asthma, and epilepsy (Access to Medicine Foundation, 2016), none of which are neglected diseases (Trouiller et al., 2002). Hence, the equitable pricing index is not directly driven by whether the company is also developing drugs for neglected diseases.

4.4 Methods

The firms in the data sample are those meeting two criteria: (1) appearing in the IMS R&D Focus data base as having at least one clinical trial for an infectious or parasitic disease between 1989 and 2013 and (2) appearing in the Compustat database which allows us to identify headquarters location and incorporate financial data. We fill in zeros for disease-years for which we do not observe clinical trials for a firm and disease after previously observing a clinical trial. We do not assign zeros for years after which the firm exited the Compustat data.

The diseases in the data sample are those for which we have disease data from the WHO global burden of disease database. In our analysis, we include all infectious and parasitic diseases in the WHO data, regardless of whether they are neglected. We define a disease as "neglected" according to the list in the seminal paper by Trouiller et al. (2002). Examples of neglected diseases include African trypanosomiasis and Chagas' disease, while examples of non-neglected diseases include Hepatitis B and HIV. We use an indicator variable to distinguish diseases that are neglected from those that are not.

We consider two measures of corporate social responsibility. First, we use clinical trials, because the trials are clearly-defined, costly, unlikely to be directly profitable, and impactful for society. Second, we use measures of equitable prices from the Access to Medicine Index.

An observation in the analysis is a firm-disease-year. The dependent variable is the count of clinical trials for a given disease d from firm f in year t. Because the dependent variable is a non-negative integer with high standard deviation, we use a general negative binomial model.

We estimate the following relationship:

$$\begin{aligned}
\text{Clinical Trials}_{d,f,t} = \exp(&\alpha_0 + \alpha_1\text{Neglected Disease}_d + \alpha_2\text{Colonial Disease Burden}_{d,f} \\
&+ \alpha_3\text{Neglected Disease x Colonial Disease Burden}_{d,f} \\
&+ \alpha_4\text{Rich Country Disease Burden}_{d,f} \\
&+ \alpha_5\text{Experience with Related Diseases}_{d,f,t-1} \\
&+ \alpha_6\text{Cumulative Basic Science Publications}_{d,t} + \phi_f + \phi_t + \epsilon)
\end{aligned} \tag{4.5}$$

We included a firm fixed effect ϕ_f and a year fixed effect ϕ_t. In another specification, we added profit and profit interacted with the neglected indicator.

Recall that we hypothesize that companies invest more if the need is high in the former colonies of their country of headquarters (Hypothesis 8). We included in the regression an indicator for neglected diseases, and we interacted the indicator with the measure of the burden of that disease in former colonies of the headquarters company.

We also hypothesized that companies would invest more if they had experience with related products (both profitable and unprofitable) (Hypothesis 9). We measured experience as lagged cumulative clinical trials in the disease area (either infectious or parasitic) subtracting the disease in question. For example, for dengue (a neglected infectious disease), we included experience with other infectious diseases (such as HIV) but excluded experience with dengue (the disease in question) and excluded experience with parasitic diseases.

Furthermore, we hypothesize that companies invest more if the potential for impact is greater due to the state of science (Hypothesis 10). We measured the state of science as cumulative basic science publications in PubMed for that disease.

Drug development is only one way in which drug manufacturers can help the global poor. Using data from the Access to Medicine Foundation, we also examined which companies helped the global poor through low drug prices (Hypothesis 11). Even companies that did not develop drugs for infectious and parasitic diseases could charge low prices for drugs for other diseases, such as heart disease and diabetes. We plot the data on equitable pricing to compare to drug development. We did not run regressions using the index because it is only available for 20 companies and 2 years. Instead, we ran regressions using only clinical trials as the dependent variable.

As a robustness check, we included profit in the regression analysis, though this reduced the sample, because we did not have profit data for all of the firms in the main regression. We added the profit rate of firm f in year t and its interaction with disease burden in its home country's past colonies as control variables in the regression. We obtained firm-year level revenue and net income/loss data from the Compustat database. We constructed the profit margin by dividing net income/loss into revenue.

4.4.1 Identification

The timing helped us avoid reverse causality. The colonial history and the headquarters location were determined before the clinical trials in our data sample. For example, Sanofi has been a French company for decades and the colonial history of France is even older.

Furthermore, we use the disease burden from the year 2000 so that clinical trials did not affect the disease burden. Clinical trials initiated at the start of our sample in 1989 were unlikely to diminish the disease burden because there is an average of an 8-year lag between clinical trial initiation and an approval (DiMasi et al., 2016) plus an additional lag between approval, access, and reduction in burden. Furthermore, if the relationship were endogenous, it would be a negative relationship (trials reducing burden) and bias against our hypothesis of a positive relationship (burden inducing trials). Finally, we included firm and year fixed effects to account for unobserved characteristics that were constant within a firm and in a given year.

4.5 Results

First we provide summary statistics on companies (Table 4.1), diseases (Table 4.2), and countries (Table 4.3). Second, we provide the results from our tests of the hypotheses (Section 4.5.2). Finally, we compare our results to another measure of corporate social responsibility (Section 4.5.3).

4.5.1 Summary statistics

There were 168 pharmaceutical companies that conducted at least 1 clinical trial for the 23 infectious and parasitic diseases included in our sample between 1989 and 2013. 41 of the companies initiated at least one clinical trial for one of the 12 neglected diseases.

The company conducting the most clinical trials for neglected diseases is Sanofi, based in France, followed by GSK, based in Britain. In a typical year, Sanofi starts more than one clinical trial for a neglected disease. GSK is second for neglected diseases and first for broad experience with all infectious and parasitic diseases (not just neglected diseases).

At the other end of the distribution, 127 companies conducted no trials for neglected diseases, despite conducting at least one trial for a commercial infectious or parasitic disease (Table 4.1).

Firms with more experience in the same class as the neglected disease tended to do more clinical trials for that disease (Table 4.1). For instance, both GSK and Pfizer, which were among top 10 firms in clinical trials for neglected diseases, had extensive research experience in infectious and parasitic diseases.

The data in our analysis include 23 diseases (15 infectious and 8 parasitic) for which we had data on the burden of the disease. Twelve (8 parasitic and 4 infectious) of the diseases were classified as neglected in the seminal paper by Trouiller et al. (2002) due to enormous burden of disease but little financial incentive to develop new treatments because most of the burden is in poor countries. Diseases with greater burden and greater cumulative knowledge of the basic science tended to have more clinical trials (Table 4.2).

Pharmaceutical companies in our sample had headquarters in 20 countries. In general, we saw a positive correlation between colonial neglected disease burden and total clinical trials for neglected diseases by companies with headquarters in the country. For example, Belgium, France, and Britain had more burden of diseases in past colonies than other countries, and firms in these two countries conducted more clinical trials for neglected diseases than firms headquartered in other countries (Figure 4.1 and Table 4.3). In Figure 4.1 we added 1 to all of the values to avoid the problem of taking the log of 0.

Our data sample consisted of 168 firms, 23 diseases, and 25 years (Table 4.4). If we had one observation for each, then our sample would have been 96,600, but we had firm-years with no observations, so we had 58,374 observations. The average firm started 0.014 clinical trials (standard deviation of 0.17) for a given disease in a year (Table 4.4).

Hence, during a decade, the average firm started 3 trials for an infectious or parasitic disease (commercial and/or neglected).

4.5.2 Results from hypotheses tests

Consistent with Hypothesis 8, companies conducted more clinical trials for a neglected disease if there is a larger burden from that disease in the former colonies of its headquarters country. We saw evidence of this effect when we plotted colonial disease burden versus clinical trials (Figure 4.1). We also saw evidence in the regression results, as indicated by the negative and statistically significant sign on the interaction between the neglected disease indication and the colonial disease burden (Table 4.5). The sign of the coefficient for the neglected indicator is negative which indicated that the diseases were properly classified as neglected.

A company would conduct 80% more clinical trials for a neglected disease if in the former colonies of its headquarters country, the disease burden (DALYs lost) is 10 million rather than 5 million.[5] While global burden of disease is positively correlated with number of clinical trials for all infectious and parasitic diseases, burden of disease in headquarters country's past colonies had no effect on clinical trials for non-neglected diseases.

As a robustness check, we also considered whether the results would change if we included the effect of company-level (rather than product-level) profit on social initiatives. Our sample size shrunk from 58,374 to 34,982, because not all companies reported their financial data across the sample period. The results were largely unchanged. The main

[5] We calculated the value using the coefficients from Table 4.5 and assuming the neglected disease had mean value of global burden, cumulated scientific publication and the sponsored firm had mean value of experience in that class.

coefficient of interest – the interaction term on neglected disease and colonial disease burden – is 0.11 without the profit control, and 0.10 with it (Table 4.5). The coefficients on profit were positive, indicating that firms with positive profits conducted more trials for neglected diseases. However, firms with positive profits tended to be larger. When accounting for firm assets, profitable firms and less profitable firms conducted approximately the same share of trials for neglected diseases.[6]

Consistent with Hypothesis 9, past experience in the same class of disease (either infectious or parasitic) is positively related to the number of clinical trial for that disease. Based on the regression results, a company would conduct 300% more clinical trials for a neglected disease if it had conducted 50 trials for related diseases than if it had conducted only 10 such trials for related diseases. For example, GSK, Merck, and Pfizer all had more than 50 trials for profitable and unprofitable infectious and parasitic diseases dating back to 1989 and all conducted research on neglected diseases.[7]

Figure 4.1 also illustrates the importance of experience. Countries with little or no colonial disease burden conducted trials for neglected diseases in part because they were already working on commercial infectious diseases. The U.S., Japan, and Switzerland all had companies based there with extensive commercial infectious disease experience. Conversely, companies based in the Netherlands had no experience in drug development for commercial infectious diseases.

Consistent with Hypothesis 10, companies tended to do more clinical trials for parasitic and infectious diseases with higher state of science. A pharmaceutical company

[6] Firms tended to remain profitable or unprofitable during the sample period. Of 1474 firm-year observations with profit status, 175 changed from non-positive to positive, or vice versa.

[7] We calculated the value using the coefficients from Table 4.5 and assuming the neglected disease has mean values for global burden and cumulative scientific publications.

would conduct 17% more clinical trials for a neglected disease if it has 5 million cumulated scientific publications instead of 1 million.

Consistent with Hypothesis 11, companies connected to developing countries not only did more drug development, but also charged lower prices. Companies with headquarters in Belgium, Britain, and France conduct more trials for neglected diseases (the horizontal axis of Figure 4.2) and charge lower prices across their entire portfolio of products (the vertical axis of Figure 4.2). For example, Britain's GSK is second highest in clinical trials for neglected diseases, with nearly one trial started per year, and rated highest on equitable pricing. The authors of the Access to Medicine Index reported that GSK's equitable pricing covered "a broad range of diseases, including HIV/AIDS, lower respiratory infections, asthma, pertussis and hypertensive heart disease" (Access to Medicine Foundation, 2016). Companies with British and French headquarters (AstraZeneca, GSK and Sanofi) scored high on equitable pricing, whereas companies with German headquarters (Boehringer and Bayer) and Japanese headquarters (Astellas, Daiichi, and Eisai) scored low (Figure 4.2). Switzerland had one high-scoring company (Novartis) and one low-scoring company (Roche).

Switzerland is an interesting case. It has no former colonies, but in the French-speaking part of Switzerland is the headquarters for the World Health Organization, the International Committee of the Red Cross, and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Hence, even without former colonies, people in the French-speaking portion of Switzerland are likely to be connected to the need for drugs for neglected diseases. Consistent with this theory, Switzerland had one high-scoring company (Novartis) in the French-speaking region and one low-scoring company (Roche) in the German-speaking region (Figure 4.2). We can also see in Figure 4.1 that Swiss firms conduct many trials for neglected diseases, perhaps because of proximity to the global health community, as well as due to the extensive experience in commercial infectious diseases, as indicated by the area of the circle in Figure 4.1.

4.5.3 Comparison to another CSR measure

Another measure of CSR is the Global 100 which is produced by Corporate Knights, a media, research and financial information products company. Corporate Knights surveyed companies with market capitalization of at least US$ 2 billion. Companies were rated on four measures of energy efficiency (including the ratio of revenue to energy use), four measures of financial performance (including the ratio of unfunded liabilities to total assets), and four measures of employee management (including the ratio of departing employees to total employees). In 2016, 7 drug companies were in the Global 100: Astellas, Johnson & Johnson, Novartis, Novo Nordisk, Sanofi, Shire, and Takeda.[8] The ratings were largely orthogonal to the measures we use. Whereas Novartis and Sanofi were two of the highest performers in both drug development and equitable pricing, Astellas and Takeda were two of the lowest performers (Figure 4.2). Whereas the CSR measures which Corporate Knights uses are based largely on efficiency and profitability, our CSR measures include inefficient and unprofitable behaviors: developing unprofitable drugs and charging prices below what the market will bear.

4.6 Conclusions

We find that a company conducts more trials for a disease if its headquarters is in a country with former colonies in which the disease is endemic. Connection to disease

[8] For complete Global 100 ratings see `http://www.corporateknights.com/reports/2016-global-100/2016-global-100-results-14533333/`.

motivates scientists, and executives know that they could better attract and retain top scientists that are doing fulfilling work.

Pharmaceutical executives and employees face public scrutiny about drug prices in the media, and perhaps even at family meals. It is surely helpful for executives and employees to tell their families about the good work they are doing. They can talk about drug development for neglected diseases that are familiar to their family members. For people in Belgium, Britain, and France, neglected diseases are not an abstract notion, because of the ties that the people have to countries in which the diseases are endemic. Recall the Belgian scientist who worked in the former Belgian colony Congo and later championed tuberculosis drug development at his company which has its headquarters in Belgium.

Executives can rationalize this form of corporate social responsibility to investors by saying that they it will be low cost, because of related research. We find that a company with experience developing commercially-viable drugs for infectious diseases (such as Hepatitis C) conducts more trials for neglected infectious diseases such as tuberculosis. Consistent with this result, Michael Porter and Mark Kramer (2006) argue that a company should work on "the particular set of societal problems that it is best equipped to help resolve."

Also, executives can rationalize social initiatives to investors by saying the company benefits from developing drugs for diseases of poverty, because poorer countries become richer over time. Indeed, emerging markets have been growing in commercial importance. While this effect is surely positive, it is also surely small. It cannot be an especially profitable strategy to lose money in sub Saharan Africa today in the hope that in the future the countries will be richer and loyal to products sold by the manufacturer. Nevertheless, the rationale might help persuade investors to not object to investments that executives and scientists want to make.

We define corporate social responsibility as development of drugs for neglected diseases. We believe this is appropriate because the medical community identifies the neglected diseases as those with enormous burden but little profit potential (Trouiller et al., 2002). Other drugs certainly benefit patients, but have profit potential.

Our study extends beyond drug development to include low prices for drugs for other diseases, such as diabetes and heart disease. We find a positive relationship between companies engaging in corporate social responsibility through drug development and companies charging equitable prices (Figure 4.2). Hence, we do not find that drug companies compensate for lack of drug development in other ways that help the global poor.

Our results suggest that companies ignore some social initiatives due to lack of concern. For example, companies with headquarters in Canada, Ireland, and Norway conduct no work on neglected diseases, though companies there work on commercial infectious and parasitic diseases. Perhaps with greater connection to the suffering caused by these diseases, the companies would invest more in neglected diseases.

Our results also suggest that governments and foundations are important for encouraging development of drugs for neglected diseases. One mechanism for encouraging drug development is to fund basic science, for example through the U.S. National Institutes of Health. Our results suggest that if scientific publications doubled, clinical trials for a disease would increase 12%.[9]

[9] Our estimate of the increase in clinical trials assumes mean values of 1.48 million for disease burden in rich countries, 0.65 million of disease burden in the home country's past colonies, and that the firm previously conducted 2 clinical trials for other infectious or parasitic diseases.

One government mechanism for encouraging drug development is the priority review voucher. The voucher is a prize worth more than \$100 million which the U.S. Food and Drug Administration (FDA) awards for successful drug development for neglected diseases (Ridley and Régnier, 2016). For prizes like the voucher, the government must determine eligibility. If the policy objective is to encourage drug development for neglected diseases at low cost, then the prize should be awarded for drugs for diseases with high burden in former colonies, because companies are predisposed to working on these diseases. However, if the policy objective is to promote equity, that is, distributing resources across diseases, then the prize should be awarded for drugs for diseases with little burden in former colonies.

Table 4.1: Descriptive statistics for companies conducting clinical trials for infectious and parasitic diseases (1989-2013)

Company Name	HQ country	Neglected clinical trials		Experience		Profit rate	
		Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
Sanofi	FRA	1.36	1.22	4.29	4.96	0.13	0.11
GlaxoSmithKline	GBR	0.79	0.83	34.48	33.53	0.19	0.04
Otsuka	JPN	0.67	0.82	0.00	0.00	n/a	n/a
Immtech	USA	0.58	0.67	0.37	0.66	−0.01	0.00
Pfizer	USA	0.54	0.88	24.83	26.77	0.19	0.09
Emergent	USA	0.50	0.71	0.00	0.00	0.03	0.03
Onxeo	FRA	0.50	0.71	1.20	1.25	n/a	n/a
Scynexis	USA	0.50	0.71	0.00	0.00	−1.07	0.83
Endo	USA	0.47	0.64	0.72	0.92	0.00	0.12
Karolinska	SWE	0.43	0.53	0.00	0.00	n/a	n/a
Janssen	BEL	0.33	0.70	14.32	15.39	0.16	0.04
Novartis	CHE	0.33	0.59	10.88	12.29	0.18	0.04
Ranbaxy	IND	0.25	0.45	0.57	0.88	n/a	n/a
Pharmstandard	RUS	0.20	0.42	0.00	0.00	n/a	n/a
Alcon	USA	0.18	0.40	0.00	0.00	0.23	0.07
AstraZeneca	GBR	0.18	0.50	4.21	2.94	0.15	0.06
Jado	DEU	0.17	0.41	0.00	0.00	n/a	n/a
Sakai	JPN	0.16	0.47	0.00	0.00	n/a	n/a
Bayer	DEU	0.14	0.36	1.96	1.59	0.05	0.03
Eisai	JPN	0.14	0.36	0.86	0.66	0.07	0.03
Roche	CHE	0.14	0.48	9.24	9.51	0.16	0.09
Agenus	USA	0.13	0.34	0.00	0.00	−0.78	2.22
Anacor	USA	0.13	0.35	0.00	0.00	−0.82	2.84
Genvec	USA	0.13	0.50	1.28	1.35	−0.23	0.64
Merck & Co	USA	0.13	0.34	20.65	23.01	0.19	0.08
Daiichi Sankyo	JPN	0.12	0.33	0.00	0.00	n/a	n/a
Takada	JPN	0.12	0.44	2.42	2.69	n/a	n/a
Chong Kun Dang	KOR	0.11	0.32	0.00	0.00	n/a	n/a
Silence Therapeutics	GBR	0.11	0.32	0.00	0.00	n/a	n/a
Valneva	FRA	0.11	0.33	0.00	0.00	n/a	n/a
Genentech	USA	0.11	0.32	4.11	3.99	0.05	0.15
Progenics	USA	0.11	0.32	0.95	0.97	−0.43	1.33
Affitech	DNK	0.10	0.32	0.54	0.92	n/a	n/a
BTG	GBR	0.10	0.44	0.63	0.92	n/a	n/a
Shin Poong	KOR	0.09	0.30	0.00	0.00	n/a	n/a
Teva	ISR	0.08	0.41	0.48	0.50	0.08	0.05
Suda	AUS	0.08	0.28	0.18	0.39	n/a	n/a
Actelion	CHE	0.07	0.26	0.03	0.16	n/a	n/a
Actelion	CHE	0.07	0.26	0.07	0.26	n/a	n/a
Mymetics	CHE	0.05	0.22	0.62	0.86	−7.92	23.08
Sciclone	USA	0.04	0.21	0.22	0.42	−1.60	5.17
Mean for 127 other firms		0.000	0.00	0.91	4.81	−5.34	63.52

Source: Authors' analysis of data from IMS Health and Compustat.
n/a indicates missing profit data in Compustat.

Table 4.2: Descriptive statistics for the diseases included in in the analysis

Disease	Type	Neglected Disease	Disease Burden (MM, DALYs, 2000) Rich Country	Poor Country	Basic Science Pubs (MM, 1989-2013)	Clinical Trials (1989-2013)
African Trypanosomiasis	Parasitic	Yes	0.01	3.74	0.42	9
Chagas' disease	Parasitic	Yes	0.23	0.57	0.67	2
Chlamydia	Infectious	No	0.55	1.28	0.68	0
Dengue	Infectious	Yes	0.07	1.01	0.5	12
Diphtheria	Infectious	No	0.04	0.49	0.2	14
Filariasis	Parasitic	Yes	0.04	2.53	0.25	0
Gonococcal	Infectious	No	0.33	0.47	0.23	3
Hepatitis B	Infectious	No	0.67	6.01	4.56	54
Hepatitis C	Infectious	No	0.04	0.85	4.56	253
HIV	Infectious	No	17.51	101.63	11.63	304
Intestinal Nematode Infections	Parasitic	Yes	2.35	6.26	0.24	0
Leishmaniasis	Parasitic	Yes	0.07	4.99	0.97	6
Leprosy	Infectious	Yes	0.09	0.22	0.23	0
Malaria	Parasitic	Yes	1.39	78.24	2.27	80
Measles	Infectious	No	0.17	55.24	0.42	6
Meningococcal	Infectious	No	2.25	41.69	0.3	30
Onchocerciasis	Parasitic	Yes	0.01	0.59	0.09	0
Rabies	Infectious	No	0.14	3.83	0.28	6
Schistosomiasis	Parasitic	Yes	0.29	3.14	0.75	1
Syphilis	Infectious	No	1.2	11.12	0.23	0
Tetanus	Infectious	No	0.29	14.94	0.29	14
Trachoma	Infectious	Yes	0.04	0.43	0.07	0
Tuberculosis	Infectious	Yes	6.33	60.29	2.73	45

DALY = Disability Adjusted Life Years. We use the definition of neglected diseases from Trouiller et al. (2002). Source: Authors' analysis of data from IMS Health, WHO, and PubMed.

Table 4.3: Descriptive statistics for countries with drug manufacturer headquarters

Country	Former Colony with Largest Neglected Disease Burden	Total Colonial Disease Burden (MM, DALYs)	Company HQ Counts	For companies with headquarters in the country: No. of Clinical Trials for Neglected Diseases	No. of Clinical Trials for Non-Neglected Infectious & Parasitic Diseases
Great Britain (GBR)	Nigeria	215	8	27	72
France (FRA)	Côte d'Ivoire	48.69	6	25	37
Belgium (BEL)	DR Congo	24.39	1	8	39
Netherland (NLD)	South Africa	19.52	1	0	3
Germany (DEU)	Rwanda	6.43	6	4	12
Italy (ITA)	Somalia	2.83	3	0	0
United States (USA)	Philippines	2.62	80	49	353
Russia (RUS)	Ukraine	2.4	1	2	0
Australia (AUS)	Papua New Guinea	0.72	6	1	12
Japan (JPN)	North Korea	0.56	18	14	66
China (CHN)	Mongolia	0.04	1	0	0
Sweden (SWE)	Estonia	0.01	5	3	6
Denmark (DNK)	Iceland	0	3	1	9
Canada (CAN)	n/a	0	5	0	9
India (IND)	n/a	0	4	3	7
Ireland (IRL)	n/a	0	4	0	1
Israel (ISR)	n/a	0	4	2	6
Korea (KOR)	n/a	0	7	3	9
Norway (NOR)	n/a	0	1	0	4
Switzerland (CHE)	n/a	0	4	11	41

DALY = Disability Adjusted Life Years. n/a indicates no former colonies. Source: Authors' analysis of data from IMS Health, WHO, and GeoDist.

Table 4.4: Summary statistics

Unit (observations)	Variable	Mean	Std Dev
Disease, Firm, Year (58,374)	Clinical Trials$_{d,f,t}$	0.01	0.17
	Experience with Related Diseases$_{d,f,t-1}$	2.00	7.94
Disease, Firm (3864)	Colonial Disease Burden$_{d,f}$ (DALY, MM)	0.65	4.31
Disease, Year (575)	Cumulative Basic Science Publications$_{d,t}$ (MM)	1.41	9.98
Firm, Year (1474)	Profit Rate$_{f,t}$	−12.79	107.98
Disease (23)	Neglected Disease$_{d}$	0.50	0.50
	Rich Country Disease Burden $_{d}$ (DALY, MM)	1.48	3.76

Disease burden measured in millions of Disability Adjusted Life Years (DALY) lost. Source: Authors' analysis of data from IMS Health, WHO, and Compustat.

Table 4.5: CSR: Regression result.

Variable	Coef.	Std Dev	Coef.	Std Dev
Neglected Disease$_{d}$ x Colonial Disease Burden$_{d,f}$(MM)	0.11***	0.02	0.10***	0.02
Neglected Disease$_{d}$	−1.09***	0.188	−1.21***	0.23
Colonial Disease Burden$_{d,f}$(MM)	0.01	0.004	0.01**	0.004
Rich Country Disease Burden$_{d}$(MM)	0.13***	0.01	0.12***	0.01
Experience with Related Diseases$_{d,f,t-1}$	0.03*	0.01	0.02	0.01
Cumulative Basic Science Publications$_{d,t}$(MM)	0.04***	0.01	0.04***	0.01
Constant	−8.64***	0.8	−8.63***	1
Neglected Disease$_{d}$ x Profit Rate$_{f,t-1}$			0.003	0.002
Profit Rate$_{f,t-1}$			0.002	0.001
Year Fixed Effects		Included		
Firm Fixed Effects		Included		
Observations	58374		34982	

Standard errors are clustered at the firm level;
$***p < 0.001$ $**p < 0.01$ $*p < 0.05$.
Disease burden measured in millions of Disability Adjusted Life Years (DALY) lost. Source: Authors' analysis of data from IMS Health, WHO, GeoDist, and PubMed.

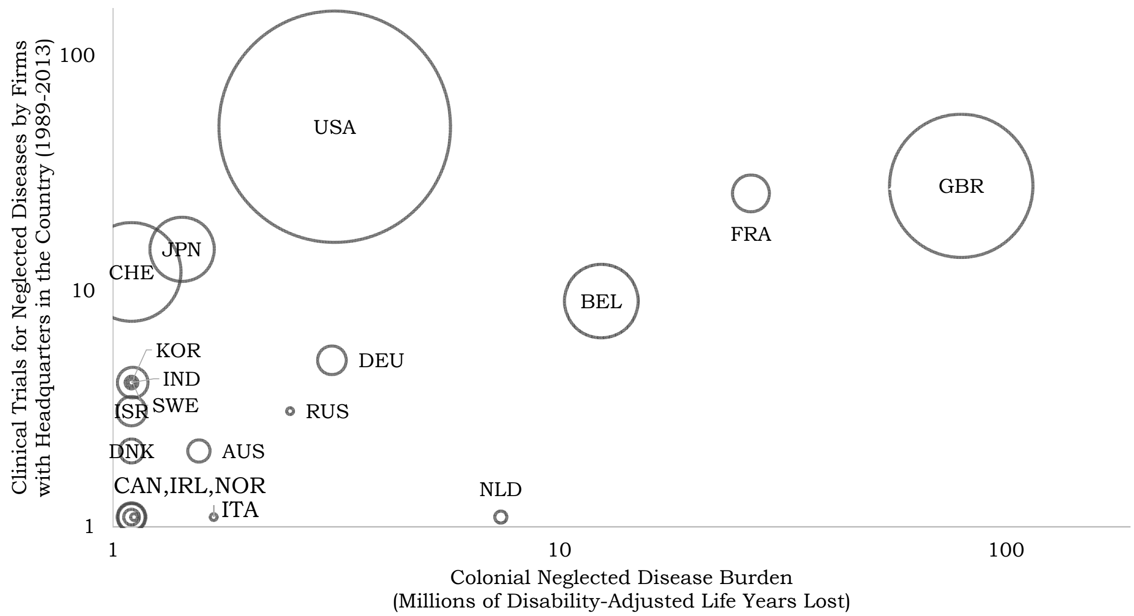

FIGURE 4.1: Experience, colonial disease burden, and clinical trial for neglected diseases.

Source: Authors' estimates using burden data from the World Health Organization and trial data from IMS Health. Country abbreviations appear in Table 4.3.

FIGURE 4.2: Equiable price index and clinical trial for neglected diseases.

Source: Authors' estimates using clinical trial data from IMS Health and ratings from the Access to Medicine Index.

5

Conclusion

The dissertation consists of three chapters relating to drug development and marketing strategies. Chapter 1 studies strategic direct-to-consumer and direct-to-physician advertising in the pharmaceutical industry. Using data from the anticholesterol market, I find pharmaceutical companies make strategic DTCA and DTP advertising by using the border strategy. Specifically, a 10% increase in DTCA expenditure per capita is associated with 0.3%-0.4% more detailing visits or 1% more detailing time for a given product in a given market. The identified positive relationship between DTP advertising and DTCA is consistent with a documented synergistic effect between these two marketing tools (Narayanan et al., 2004). To further understand the source of the synergistic effect, I construct and estimate a demand model that explicitly models patients' and physicians' decisions about requesting and prescribing brand-name medications considering the impacts from pharmaceutical advertising. I find DTCA encourages patients to visit their physicians and encourages patients with private healthcare insurance to request the advertised brand; physicians value patients' request and are more likely to prescribe the requested brand; and DTP advertising boosts the number of prescriptions for the advertised brand, whether the brand is requested by the patient or not. Simulation results show that comparing to patient visit, patient request for a brand-name medication is the primary channel through which DTCA affects patients and is the source of the synergistic effect between DTCA and DTP advertising. These findings have both advertising strategy and healthcare policy implications. Pharmaceutical firms might be able to realize more gains by coordinating DTCA and DTP advertising than if they fail to coordinate these efforts. Moreover, regulators should consider the connection between DTCA and DTP advertising when making policies, otherwise regulatory policies might lead to unintended or even opposing consequences.

Chapter 2 examines the strategic interaction between government agencies in funding support for medical research. In this chapter we document how governments respond to other funders in supporting medical research. First, we show a negative correlation between outlays for a disease by the US government and outlays by other governments, NGOs, and foundations in the following year, while accounting for the endogeneity of US outlays. We also find that in Latin America and the Caribbean, HIV/AIDS imposed the greatest disease burden, but received less in total funding outlays than diseases like Chagas and dengue. Indeed, the government of Brazil spent less on HIV/AIDS research than on Chagas and dengue research, even though Brazil's disease burden from HIV/AIDS was 100 times greater than the burden from Chagas and dengue. Documenting government responses to changes in medical research funding outlays is relevant to both research and policy sectors. Scholars should be aware that estimates of the impact of one additional dollar of NIH funding could underestimate the effect, because the net increase in funding for that disease will be smaller. Policy makers should be aware of how governments adjust funding and consider enhancing international coordination, regardless of whether the negative relationship across funders is socially optimal. The evidence in this paper suggests that governments should increase efforts to coordinate on medical R&D funding through organizations such as the World Health Organization as they do in other areas, including military defense and environmental regulation.

Chapter 3 investigates how pharmaceutical companies make R&D decisions for neglected diseases. We find that a company conducts more trials for a disease if its headquarters is in a country with former colonies in which the disease is endemic. Connection to disease motivates scientists, and executives know that they could better attract and retain top scientists that are doing fulfilling work. Our results suggest that companies ignore some social initiatives due to lack of concern. For example, companies with headquarters in Canada, Ireland, and Norway conduct no work on neglected diseases, though companies there work on commercial infectious and parasitic diseases. Perhaps with greater connection to the suffering caused by these diseases, the companies would invest more in neglected diseases. Our results also suggest that governments and foundations are important for encouraging development of drugs for neglected diseases. One mechanism for encouraging drug development is to fund basic science, for example through the U.S. National Institutes of Health. Our results suggest that if scientific publications doubled, clinical trials for a disease would increase 12%.

Appendix A

Strategic DTCA and DTP advertising

In this section I formally derive the four hypotheses listed in section 2.4.4. Taking derivative of the first order derivative of market share with respect to DTP advertising with respect to DTCA , we have

$$\frac{\partial s_{kmt}}{\partial DTP_{pkt}\partial DTCA_{mkt}} =\gamma^r\gamma^v\gamma^p P(Y) M_{mkt}R_{kt}s^v_{mt}[\frac{(1-s^v_{mt})s^r_{mkt}}{DTC_{mkt}}\frac{\sum_{k'} s^r_{mk't}s^p_{m,k|k',t}(1-s^p_{m,k|k',t})}{DTP_{mkt}}]+$$

$$\gamma^r M_{mkt}R_{kt}s^v_{mt}[\frac{\gamma^p s^r_{mkt}(1-s^r_{mkt})s^p_{m,k|k,t}(1-s^p_{m,k|k,t})}{DTC_{mkt}DTP_{mkt}}$$

$$-\frac{\sum_{k'\neq k} s^r_{mkt}(1-s^r_{mkt})s^p_{m,k|k',t}(1-s^p_{m,k|k',t})}{DTC_{mkt}DTP_{mkt}}]$$

Let $F = \frac{\partial s_{kmt}}{\partial DTP_{pkt}\partial DTCA_{mkt}}$. It is straight forward to show that $F \leqslant 0$ if $\gamma^r \leqslant 0$ (Hypothesis 1).

In addition, because $-\frac{\sum\limits_{k' \neq k} s^r_{mkt}(1-s^r_{mkt})s^p_{m,k|k',t}(1-s^p_{m,k|k',t})}{DTC_{mkt}DTP_{mkt}} \leqslant 0$, $F \leqslant 0$ if $\gamma^p \leqslant 0$ (Hypothesis 2).

Next, take derivative of F with respect to $\gamma^v > 0$, we have

$$\frac{\partial F}{\gamma^v} = \gamma^r \gamma^p P(Y) s^v_{mt} [\frac{(1 - s^v_{mt}) s^r_{mkt}}{DTC_{mkt}} \frac{\sum\limits_{k'} s^r_{mk't} s^p_{m,k|k',t}(1 - s^p_{m,k|k',t})}{DTP_{mkt}}] \geqslant 0$$

Thus, the synergy effects between DTCA and DTP advertising is non-decreasing with γ^v.

Finally, take derivative of F with respect to θ_p, we have

$$\begin{aligned}
\frac{\partial F}{\theta^p} &= \gamma^r \gamma^p \gamma^v s^v_{mt} [\frac{(1 - s^v_{mt}) s^r_{mkt}}{DTC_{mkt}} \frac{\sum\limits_{k'} s^r_{mk't} s^p_{m,k|k',t}(1 - s^p_{m,k|k',t})}{DTP_{mkt}}] \frac{\partial P(Y)}{\partial \theta^p} \\
&= \gamma^r \gamma^p \gamma^v s^v_{mt} [\frac{(1 - s^v_{mt}) s^r_{mkt}}{DTC_{mkt}} \frac{\sum\limits_{k'} s^r_{mk't} s^p_{m,k|k',t}(1 - s^p_{m,k|k',t})}{DTP_{mkt}}] \text{Prob}(k|A^c_{ikt} = 1)(1 - \text{Prob}(k|A^c_{ikt} = 1)) \\
&\geqslant 0
\end{aligned}$$

Thus, the synergy effects between DTCA and DTP advertising is non-decreasing with θ_p.

Appendix B

A theoretical model of strategic funding decision

Consider a simple version of the model with two funders, i and j, two diseases, a and b, and an outside option o^f, which is specific to a funder. Assume two stages. In stage one, funder i distributes funding across diseases based on the burden of disease that can be alleviated B and scientific knowledge S, while ignoring outlays from the fringe funder j. In stage two, funder j distributes funding according to its local disease burden, scientific knowledge, and the funding from funder i.

The dominant funder chooses outlays without regard to outlays by the fringe funder. The dominant funder model seems appropriate in our context for two reasons. First, the US government accounts for the majority of global funding for 15 infectious and parasitic diseases in our analysis, while the median funder in our sample accounts for less than 1 percent of overall funding (Table 3.2). The combination of NIH and Gates Foundation accounts for 70 percent of funding. Second, we could find no evidence that the NIH or other government agencies factor in the behavior of non-US funders. Consistent with our model, NIH leaders quoted in the text described funding priorities based on disease burden and scientific knowledge without mention of other funders (Rockey and Wolinetz, 2015). In contrast, other funders often mention that they are filling perceived gaps. Recall the quote from a program officer of the Burroughs Wellcome Fund who described avoiding funding of areas that the US government funds.

Following the innovation economics literature, we assume the production function of treatment, $g(\sum_f x_d^f, S_d) = S_d(1 - e^{-\sum_f x_d^f})$ (Loury, 1979; Reinganum, 1982). Also, we assume $h(o^f) = 1 - e^{-o^f}$, but our results are robust to other functional forms of $h(o^f)$. Under these assumptions, we can rewrite the objective function of funder i (Equation 3.1) as

$$\max_{x_d^i} B_a S_a(1 - e^{-x_a^i}) + B_b S_b(1 - e^{-x_b^i}) + (1 - e^{-o^i})$$
$$s.t. : x_a^i + x_b^i + o^i = Y^i, \tag{B.1}$$

The optimal funding distribution for funder i is summarized by three equations:

$$x_a^{i*} = \frac{Y^i + 2\log(B_a S_a) - \log(B_b S_b)}{3} \tag{B.2}$$

$$x_b^{i*} = \frac{Y^i - \log(B_a S_a) + 2\log(B_b S_b)}{3} \tag{B.3}$$

$$o^{i*} = \frac{Y^i - \log(B_a S_a) - \log(B_b S_b)}{3} \tag{B.4}$$

It is straightforward to show that

$$
\begin{aligned}
\frac{\partial x_a^{i*}}{\partial B_a} &= \frac{2}{3B_a} > 0 \\
\frac{\partial x_a^{i*}}{\partial S_a} &= \frac{2}{3S_a} > 0,
\end{aligned}
\tag{B.5}
$$

which suggests that the dominant funder i provides greater outlays for diseases with higher burdens and/or diseases with higher scientific knowledge.

Now we solve for the optimal outlays by the fringe funder j. The objective function for the fringe funder j, when funder j considers local disease burden only, is:

$$
\begin{gathered}
\max_{x_d^j} B_a^j S_a(1 - e^{-x_a^{i*} - x_a^j}) + B_b^j S_b(1 - e^{-x_b^{i*} - x_b^j}) + (1 - e^{-o^i}) \\
s.t. : x_a^j + x_b^j + o^j = Y^j,
\end{gathered}
\tag{B.6}
$$

The optimal outlays by funder j, given the funding from funder i, are:

$$
x_a^{j*} = \frac{Y^j - 2x_a^{i*} + x_b^{j*} + 2\log(B_a^j S_a) - \log(B_b^j S_b)}{3} \tag{B.7}
$$

$$
x_b^{j*} = \frac{Y^j - 2x_b^{i*} + x_a^{i*} - \log(B_a^j S_a) + 2\log(B_b^j S_b)}{3} \tag{B.8}
$$

$$
o^{j*} = \frac{Y^j + x_b^{i*} + x_a^{i*} + \log(B_a^j S_a) + \log(B_b^j S_b)}{3} \tag{B.9}
$$

Now we consider how the fringe funder j responds to changes in outlays by the dominant funder i.

$$\frac{\partial x_a^{j*}}{\partial x_a^{i*}} = \frac{\partial x_b^{j*}}{\partial x_b^{i*}} = -\frac{2}{3} < 0 \tag{B.10}$$

and

$$\frac{\partial x_a^{j*}}{\partial x_b^{i*}} = \frac{\partial x_b^{j*}}{\partial x_a^{i*}} = \frac{1}{3} > 0 \tag{B.11}$$

Thus, greater outlays for a disease by the dominant funder will reduce outlays for the disease by the fringe funder (Hypothesis 6) and increase outlays for a different disease by the fringe funder (Hypothesis 7).

In addition, we have

$$\frac{\partial x_a^{j*} + x_b^{j*}}{\partial x_b^{i*}} = \frac{\partial x_a^{j*} + x_b^{j*}}{\partial x_a^{i*}} = -\frac{1}{3} < 0. \tag{B.12}$$

In other words, increased outlays by the dominant funder would induce the fringe funder to invest less in global diseases overall (Hypothesis 7).

Finally, we briefly discuss how exogenous shocks to disease burden, scientific knowledge, and the budget of funders affect the funding decision of funder f, and explain the importance of using instrumental variables for identification with a simple example. We start with disease burden and scientific foundation. As in equation B.12, we have

$$\begin{aligned} \frac{\partial x_a^{j*}}{\partial B_a^j} &= \frac{2}{3B_a^j} - \frac{5}{9B_a} > 0 \\ \frac{\partial x_a^{j*}}{\partial S_a^j} &= \frac{1}{9S_a} > 0, \end{aligned} \tag{B.13}$$

which suggests that like the dominant funder i, the fringe funder j provides more funding for disease with a greater burden and/or scientific knowledge (Hypothesis 5).

Next we examine how the funding support from funder j responds to a positive shock to the budget of funder i. From equation B.7 and B.8 we have:

$$\begin{aligned}\frac{\partial x_a^{j*}}{\partial Y^i} &= -2\frac{\partial x_a^{i*}}{\partial Y^i} + \frac{\partial x_b^i}{\partial Y^i} = -\frac{1}{3} < 0 \\ \frac{\partial x_b^{j*}}{\partial Y^i} &= -2\frac{\partial x_b^{i*}}{\partial Y^i} + \frac{\partial x_a^i}{\partial Y^i} = -\frac{1}{3} < 0.\end{aligned} \tag{B.14}$$

In other words, a positive shock to the budget of funder i would induce lower funding support for both disease a and b from funder j through increasing funding support from funder i itself.

Finally, we show why we need an instrumental variable for identification. Consider a global economic shock that increases the budget of both funder i and funder j. For simplicity, we assume that the budget of funder i increases one unit, and the budget of funder j increases two units. In this case, the overall changes in x_a^{i*} and x_b^{i*} are

$$\begin{aligned}\frac{\partial x_a^{i*}}{\partial Y^i} &= \frac{1}{3} > 0 \\ \frac{\partial x_b^{i*}}{\partial Y^i} &= \frac{1}{3} > 0.\end{aligned} \tag{B.15}$$

Accordingly, the overall changes in x_a^{j*} and x_b^{j*} are

$$\begin{aligned}\frac{\partial x_a^{j*}}{\partial Y^j} + \frac{\partial x_a^{j*}}{\partial Y^i} &= \frac{2}{3} - \frac{1}{3} = \frac{1}{3} > 0 \\ \frac{\partial x_b^{j*}}{\partial Y^j} + \frac{\partial x_a^{j*}}{\partial Y^i} &= \frac{2}{3} - \frac{1}{3} = \frac{1}{3} > 0.\end{aligned} \tag{B.16}$$

Thus, the shock increases funding support for disease a and b globally. As a result, x_a^{i*} and x_a^{j*} (x_b^{i*} and x_b^{j*}) would be positively correlated in the data, contrary to the theoretical prediction, as displayed in equation B.10. Hence, we need an instrumental variable that affects the outlays of only one funder.

Appendix C

A theoretical model of corporate social responsibility

Recall from section 4.2 that the executive's utility function includes three terms. The first term is revenue and the second term is consumer surplus multiplied by $0 \leqslant \alpha \leqslant 1$ which is the amount that the firm cares about consumer surplus. The third term is the investment cost. The investment x appears in each of the three terms: greater investment increases revenue, consumer surplus, and cost. We assume quadratic costs and we assume linear demand: $Q = (1 - p)$.

$$u(p, x) = xp(1 - p) + \alpha x(1/2)(1 - p)^2 - (x^2)/\kappa x_i$$

First, the firm chooses its investment x and then its price p to maximize utility. We solve backward, beginning with the price and then solving investment conditional on price. The solutions are as follows:

$$
\begin{aligned}
x^* &= \kappa x_i/(4(2-\alpha)) \\
p^* &= (1-\alpha)/(2-\alpha)
\end{aligned}
$$

We can now differentiate the utility-maximizing values with respect to the parameters to consider some comparative statics.

$$
\delta x^*/\delta\alpha = \kappa x_i/(4(2-\alpha)^2) > 0 \tag{C.1}
$$

$$
\delta x^*/\delta x_i = \kappa/(4(2-\alpha)) > 0 \tag{C.2}
$$

$$
\delta x^*/\delta\kappa = x_i/(4(2-\alpha)) > 0 \tag{C.3}
$$

$$
\delta p^*/\delta\alpha = -1/(2-\alpha)^2 < 0 \tag{C.4}
$$

These results are consistent with our hypotheses. We can see that x is increasing in α, x_i, and κ. (Recall that $0 \leqslant \alpha \leqslant 1$). We can also see that p is decreasing in α.

Bibliography

Access to Medicine Foundation (2016), "Access to Medicine Index," .

Acemoglu, D., Johnson, S., and Robinson, J. A. (2001), "The Colonial Origins of Comparative Development: An Empirical Investigation," *American Economic Review*, 91, 1369–1401.

Alcácer, J. and Zhao, M. (2012), "Local R&D Strategies and Multilocation Firms: The Role of Internal Linkages," *Management Science*, 58, 734–753.

Andreoni, J. and Payne, A. A. (2011), "Is Crowding Out Due Entirely to Fundraising? Evidence from a Panel of Charities," *Journal of Public Economics*, 95, 334–343.

Azoulay, P. (2002), "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics & Management Strategy*, 11, 551–594.

Baron, D. P. (2007), "Corporate Social Responsibility and Social Entrepreneurship," *Journal of Economics & Management Strategy*, 16, 683–717.

Baron, D. P. (2008), "Managerial Contracting and Corporate Social Responsibility," *Journal of Public Economics*, 92, 268–288.

Berndt, E. R. (2005), "To Inform or Persuade? Direct-to-Consumer Advertising of Prescription Drugs," *The New England Journal of Medicine*, 352, 325–328.

Berndt, E. R., Glennerster, R., Kremer, M. R., Lee, J., Williams, H., Levine, R., and Weizsa, G. (2007), "Advance Market Commitments for Vaccines Against Neglected Diseases: Estimating Costs and Effectiveness," *Health Economics*, 511, 491–511.

Bloom, N., Schankerman, M., and Van Reenen, J. (2013), "Identifying Technology Spillovers and Product Market Rivalry," *Econometrica*, 81, 1347–1393.

Blume-Kohout, M. E. (2012), "Does Targeted, Disease-Specific Public Research Funding Influence Pharmaceutical Innovation?" *Journal of Policy Analysis and Management*, 31, 641–660.

Britten, N., Stevenson, F. A., Barry, C. A., Barber, N., Bradley, P., Britten, N., Stevenson, F. A., Barry, C. A., Barber, N., and Bradley, C. P. (2000), "Misunderstandings in Prescribing Decisions in General Practice: Qualitative Study," *BMJ: British Medical Journal*, 320, 484–488.

Brueckner, J. K. (2003), "Strategic Interaction Among Governments: An Overview of Empirical Studies," *International Regional Science Review*, 26, 175–188.

Burbano, V. C. (2016), "Social responsibility messages and worker wage requirements: Field experimental evidence from online labor marketplaces," *Organization Science*, 27, 1010–1028.

Case, A. C., Rosen, S., and Hines, J. R. (1993), "Budget Spillovers Interdependence: Evidence and Fiscal Policy from the States," *Journal of Public Economics*, 52, 285–307.

Center for Postsecondary Research (2016), "Carnegie Classifications 2015 public data file," .

Chatterji, A. K., Levine, D. I., and Toffel, M. W. (2009), "How Well Do Social Ratings Actually Measure Corporate Social Responsibility?" *Journal of Economics & Management Strategy*, 18, 125–169.

Chatterji, A. K., Kim, J., and McDevitt, R. C. (2017), "School Spirit: Legislator School Ties and State Funding for Higher Education," *Duke University working paper*.

Chaudhuri, S., Goldberg, P. K., and Jia, P. (2006), "Estimating the Effects of Global Patent Protection in Pharmaceuticals: A Case Study of Quinolones in India," *American Economic Review*, 96, 1477–1514.

Cheng, B., Ioannou, I., and Serafeim, G. (2014), "Corporate Social Responsibility and Access to Finance," *Strategic Management Journal*, 35, 1–23.

Ching, A. and Ishihara, M. (2010), "The Effects of Detailing on Prescribing Decisions under Quality Uncertainty," *Quantitative Marketing and Economics*, 8, 123–165.

Ching, A. T. and Ishihara, M. (2012), "Measuring the Informative and Persuasive Roles of Detailing on Prescribing Decisions," *Management Science*, 58, 1374–1387.

Ching, A. T., Clark, R., Horstmann, I., and Lim, H. (2016), "The Effects of Publicity on Demand: The Case of Anti-Cholesterol Drugs," *Marketing Science*, 35, 158–181.

Chintagunta, P. K., Goettler, R. L., and Kim, M. (2012), "New Drug Diffusion When Forward-Looking Physicians Learn from Patient Feedback and Detailing," *Journal of Marketing Research*, 49, 807–821.

Cohen, L., Coval, J. D., and Malloy, C. (2011), "Do Powerful Politicians Cause Corporate Downsizing?" *Journal of Political Economy*, 119, 1015–1060.

Cohen, W. M. and Levinthal, D. A. (1990), "Absorptive capacity: A new perspective on learning and innovation," *Administrative Science Quarterly*, 35, 128–152.

Cutler, D. M. and Gruber, J. (1996), "Does Public Insurance Crowd out Private Insurance?" *The Quarterly Journal of Economics*, 111, 391–430.

David, P. A., Hall, B. H., and Toole, A. A. (2000), "Is Public R&D a Complement or Substitute for Private R&D? A Review of the Econometric Evidence," *Research Policy*, 29, 497–529.

de Figueiredo, J. M. and Silverman, B. S. (2006), "Academic Earmarks and the Returns to Lobbying," *The Journal of Law & Economics*, 49, 597–625.

de Frutos, M. A., Ornaghi, C., and Siotis, G. (2013), "Competition in the Pharmaceutical Industry: How Do Quality Differences Shape Advertising Strategies?" *Journal of Health Economics*, 32, 268–285.

Delmas, M. A. and Toffel, M. W. (2008), "Organizational responses to environmental demands: Opening the black box," *Strategic Management Journal*, 29, 1027–1055.

Dentzer, S. (2009), "Eliminating neglected diseases in poor countries: A conversation with Andrew Witty," *Health Affairs*, 28, w411———w416.

DiMasi, J. A., Grabowski, H. G., and Hansen, R. W. (2016), "Innovation in The Pharmaceutical Industry: New Estimates of R&D Costs," *Journal of Health Economics*, 47, 20–33.

Division, C., Cen, M. C., and Guzman, D. (2013), "Physician Acquiescence to Patient Demands for Brand-Name Drugs: Results of a National Survey of Physicians," *JAMA Internal Medicine*, 173, 237–239.

Duggan, M., Garthwaite, C., and Goyal, A. (2016), "The Market Impacts of Pharmaceutical Product Patents in Developing Countries: Evidence from India," *American Economic Review*, 106, 99–135.

Ellison, G. and Ellison, S. F. (2011), "Strategic Entry Deterrence and the Behavior of Pharmaceutical Incumbents Prior to Patent Expiration," *American Economic Journal: Microeconomics*, 3, 1–36.

et al. Fitchett, J. R. A. (2016), "Ebola research funding: A systematic analysis, 1997–2015," *Journal of Global Health*, 6.

Fabrizio, K. R. (2009), "Absorptive capacity and the search for innovation," *Research Policy*, 38, 255–267.

Fabrizio, K. R. and Thomas, L. G. (2012), "The Impact of Local Demand on Innovation in a Global Industry," *Strategic Management Journal*, 33, 42–64.

Fang, H. and Rizzo, J. A. (2009), "Competition and Physician-enabled Demand: The Role of Managed Care," *Journal of Economic Behavior & Organization*, 72, 463–474.

Flammer, C. (2015a), "Does Corporate Social Responsibility Lead to Superior Financial Performance? A Regression Discontinuity Approach," *Management Science*, 61, 2568–2579.

Flammer, C. (2015b), "Does Product Market Competition Foster Corporate Social Responsibility? Evidence from Trade Liberalization," *Strategic Management Journal*, 36, 1469–1485.

Flammer, C. and Luo, J. (2017), "Corporate social responsibility as an employee governance tool: Evidence from a quasi-experiment," *Strategic Management Journal*, 38, 163–183.

Frantsve, L. M. E. and Kerns, R. D. (2007), "Patient Provider Interactions in the Management of Chronic Pain: Current Findings within the Context of Shared Medical Decision Making," *Pain Medicine*, 8, 25–35.

Freeman, R. E. (1984), *Strategic Management: A Stakeholder Approach*, Pitman, Boston.

Friedman, M. (1970), "The Social Responsibility of Business Is To Increase Its Profits," *The New York Times Magazine*.

Furman, J. L. (2003), "Location and organizing strategy: Exploring the influence of location on the organization of pharmaceutical research," in *Advances in Strategic Management*, eds. J. A. C. Baum and O. Sorenson, pp. 49–87, Emerald Group Publishing Limited.

Furman, J. L., Murray, F., and Stern, S. (2012), "Growing Stem Cells: The Impact of Federal Funding Policy on the U.S. Scientific Frontier," *Journal of Policy Analysis and Management*, 31, 661–705.

Gagnon, M. A. and Lexchin, J. (2008), "The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States," *PLoS Medicine*, 5, 29–33.

Goolsbee, A. (1998), "Does R&D Policy Primarily Benefit Scientists and Engineers?" *American Economic Review*, 88, 298–302.

Gregory, R., Peters, E., and Slovic, P. (2011), "Making Decisions About Prescription Drugs: A Study of Doctor-patient Communication," *Health, Risk & Society*, 13, 347–371.

Gruber, J. and Hungerman, D. M. (2007), "Faith-Based Charity and Crowd-Out during the Great Depression," *Journal of Public Economics*, 91, 1043–1069.

Gruber, J. and Simon, K. (2008), "Crowd-Out 10 Years Later: Have Recent Public Insurance Expansions Crowded Out Private Health Insurance?" *Journal of Health Economics*, 27, 201–217.

Hegde, D. (2009), "Political Influence behind the Veil of Peer Review: An Analysis of Public Biomedical Research Funding in the United States," *The Journal of Law and Economics*, 52, 665–690.

Hegde, D. and Mowery, D. C. (2008), "Politics and Funding in the U.S. Public Biomedical R&D System," *Science*, 322, 1797–1798.

Holburn, G. L. F. and Zelner, B. A. (2010), "Political Capabilities, Policy Risk, and International Investment Strategy: Evidence from the Global Electric Power Generation Industry," *Strategic Management Journal*, 1315, 1290–1315.

Hong, B., Li, Z., and Minor, D. (2016), "Corporate Governance and Executive Compensation for Corporate Social Responsibility," *Journal of Business Ethics*, 136, 199–213.

Husted, B. W., Jamali, D., and Saffar, W. (2016), "Near and Dear? The Role of Location in CSR Engagement," *Strategic Management Journal*, 37, 2050–2070.

Iizuka, O. and Jin, G. Z. (2005), "The Effect of Prescription Drug Advertising on Doctor Visits," *Journal of Economics and Management Strategy*, 14, 701–727.

Iizuka, T. (2004), "What Explains the Use of Direct-to-consumer Advertising of Prescription Drugs?" *Journal of Industrial Economics*, 52, 349–379.

Ioannou, I. and Serafeim, G. (2015), "The Impact of Corporate Social Responsibility on Investment Recommendations: Analysts' Perceptions and Shifting Institutional Logics," *Strategic Management Journal*, 36, 1053–1081.

Jayawardhana, J. (2013), "Direct-to-consumer Advertising and Consumer Welfare," *International Journal of Industrial Organization*, 31, 164–180.

Jones, T. M. (1995), "Instrumental stakeholder theory: A synthesis of ethics and economics," *Academy of Management Review*, 20, 404–437.

Keyhani, S., Wang, S., Hebert, P., Carpenter, D., and Anderson, G. (2010), "US Pharmaceutical Innovation in an International Context," *American Journal of Public Health*, 100, 1075–1080.

Kremer, M. R. (2002), "Pharmaceuticals and the Developing World," *Journal of Economic Perspectives*, 16, 67–90.

Kuklina, E. V., Carroll, M. D., Shaw, K. M., and Hirsch, R. (2013), "Trends in High LDL Cholesterol, Cholesterol-lowering Medication Use, and Dietary Saturated-fat Intake: United States, 1976-2010." *NCHS data brief*, pp. 1–8.

Kyle, M. K. (2006), "The Role of Firm Characteristics in Pharmaceutical Product Launches," *RAND Journal of Economics*, 37, 602–618.

Kyle, M. K. and McGahan, A. M. (2012), "Investments in Pharmaceuticals Before and After TRIPS," *Review of Economics and Statistics*, 94, 1157–1172.

Lee, D. R. (1988), "Free Riding and Paid Riding in the Fight Against Terrorism," *The American Economic Review*, 78, 22–26.

Lichtenberg, F. R. (2001), "The Allocation of Publicly Funded Biomedical Research," in *Medical Care Output and Productivity*, eds. D. M. Cutler and E. R. Berndt, pp. 565–590, University of Chicago Press.

Liu, Q. and Gupta, S. (2011), "The impact of direct-to-consumer advertising of prescription drugs on physician visits and drug requests : Empirical findings and public policy implications," *International Journal of Research in Marketing*, 28, 205–217.

Liu, Q., Gupta, S., Venkataraman, S., and Liu, H. (2015), "An Empirical Model of Drug Detailing: Dynamic Competition and Policy Implications," *Management Science*, 62, 1–20.

Loury, G. C. (1979), "Market Structure and Innovation," *The Quarterly Journal of Economics*, 93, 395–410.

Madsen, P. M. and Rodgers, Z. J. (2015), "Friends, acquaintances, or strangers? Partner selection in R&D alliances," *Strategic Management Journal*, 36, 776–794.

Makoul, G., Arntson, P., and Schofield, T. (1995), "Health Promotion in Primary Care: Physician-patient Communication and Decision Making About Prescription Medications," *Social Science & Medicine*, 41, 1241–1254.

Manchanda, P. and Chintagunta, P. (2004), "Behavior of Physician Prescription Responsiveness to Salesforce Effort: An Individual Level Analysis," *Marketing Letters*, 15, 129–145.

McClellan, M. C. (2003), "Speech before First International Colloquium on Generic Medicine," .

McKinlay, J. B., Trachtenberg, F., Marceau, L. D., Katz, J. N., and Fischer, M. A. (2014), "Effects of Patient Medication Requests on Physician Prescribing Behavior: Results of A Factorial Experiment," *Medical Care*, 52, 294–299.

McNeil, D. G. (2010), "Ally for the Poor in an Unlikely Corner," *The New York Times*.

Mintz, J. and Tulkens, H. (1986), "Commodity Tax Competition between Member States of a Federation: Equilibrium and Efficiency," *Journal of Public Economics*, 29, 133–172.

Moran, M. (2010), "Funding for Research and Development and the Financial Crisis," *Lancet Infectious Diseases*, 10, 214–215.

Murdoch, J. C. and Sandler, T. (1984), "Complementarity, Free Riding, and the Military Expenditures of NATO Allies," *Journal of Public Economics*, 25, 83–101.

Murdoch, J. C. and Sandler, T. (1997), "The Voluntary Provision of a Pure Public Good: The Case of Reduced CFC Emissions and the Montreal Protocol," *Journal of Public Economics*, 63, 331–349.

Murray, F. (2013), "Evaluating the Role of Science Philanthropy in American Research Universities," *Innovation Policy and the Economy*, 13, 23–60.

Narayanan, S., Desiraju, R., and Chintagunta, P. K. (2004), "Return on Investment Implications for Pharmaceutical Promotional Expenditures : The Role of Marketing-Mix Interactions," *Journal of Marketing*, 68, 90–105.

Narayanan, S., Manchanda, P., and K, P. (2005), "Temporal Differences in the Role of Marketing Communication in New Product Categories," *Journal of Marketing Research*, XLII, 278–291.

National Academies of Sciences, Engineering, and Medicine (2016), *Evaluation of the Congressionally Directed Medical Research Programs Review Process*, The National Academies Press, Washington, DC.

Nordhaus, W. (2015), "Climate Clubs: Overcoming Free-riding in International Climate Policy," *The American Economic Review*, 105, 1339–1370.

Olson, M. and Zeckhauser, R. (1966), "An Economic Theory of Alliances," *The Review of Economics and Statistics*, 48, 266–279.

Porter, M. E. and Kramer, M. R. (2006), "Strategy and society: The link between corporate social responsibility and competitive advantage," *Harvard Business Review*, 84, 78–92.

Porter, M. E. and Stern, S. (2001), "Innovation: Location Matters," *MIT Sloan Management Review*, 42, 28–36.

Prosser, H., Almond, S., and Walley, T. (2003), "Influences on GPs ' Decision to Prescribe New Drugs the Importance of Who Says What," *Family Practice*, 20, 61–68.

Reinganum, J. F. (1982), "A Dynamic Game of R&D: Patent Protection and Competitive Behavior," *Econometrica*, 50, 671–688.

Ridley, D. B. (2015), "Payment, Promotition, and The Purple Pill," *Health Economics*, 24, 86–102.

Ridley, D. B. and Régnier, S. A. (2016), "The Commercial Market for Priority Review Vouchers," *Health Affairs*, 35, 776–783.

Roberts, R. D. (1984), "A Positive Model of Private Charity and Public Transfers," *Journal of Political Economy*, 92, 136–148.

Rockey, S. and Wolinetz, C. (2015), "Burden of Disease and NIH Funding Priorities," *NIH Extramural Nexus*.

Rosenkopf, L. and Nerkar, A. (2001), "Beyond local search: Boundary-spanning, exploration, and impact in the optical disk industry," *Strategic Management Journal*, 22, 287–306.

Røttingen, J.-A., Regmi, S., Eide, M., Young, A. J., Viergever, R. F., Ardal, C., Guzman, J., Edwards, D., Matlin, S. a., and Terry, R. F. (2013), "Mapping of Available Health Research and Development Data: What's There, What's Missing, and What Role Is There for a Global Observatory?" *Lancet*, 382, 1286–1307.

Safran, D. G., Montgomery, Jana, E., Chang, H., Murphy, J., and Rogers, W. H. (2001), "Switching Doctors: Predictors of Voluntary Disenrollment from a Primary Physician's Practice," *The Journal of Family Practice*, 50, 130–135.

Sandler, T. and Murdoch, J. C. (1990), "Nash-Cournot or Lindahl Behavior?: An Empirical Test for the NATO Allies," *The Quarterly Journal of Economics*, 105, 875–894.

Scherer, F. M. (1993), "Pricing, Profits, and Technological Progress in the Pharmaceutical Industry," *Journal of Economic Perspectives*, 7, 97–115.

Shan, L., Fu, S., and Zheng, L. (2016), "Corporate Sexual Equality and Firm Performance," *Strategic Management Journal*.

Shapiro, B. T. (2017), "Positive Spillovers and Free Riding in Advertising of Prescription Pharmaceuticals: The Case of Antidepressants," *Journal of Political Economy*, 126, 695475.

Shih, Y.-c. T. and Tai-seale, M. (2012), "Physicians' Perception of Demand-induced Supply in the Information Age : A Latent Class Model Analysis," *Health Economics*, 21, 252–269.

Shiu, Y.-M. and Yang, S.-L. (2017), "Does engagement in corporate social responsibility provide strategic insurance-like effects?" *Strategic Management Journal*, 38, 455–470.

Siegel, D. S. and Vitaliano, D. F. (2007), "An Empirical Analysis of the Strategic Use of Corporate Social Responsibility," *Journal of Economics & Management Strategy Management Strategy*, 16, 773–792.

Sinkinson, M. and Starc, A. (2015), "Ask Your Doctor? Direct-to-Consumer Advertising of Pharmaceuticals," *NBER Working Paper 21045*.

Stern, S. (2004), "Do Scientists Pay to Be Scientists?" *Management Science*, 50, 835–853.

Stevenson, F. A., Barry, C. A., Britten, N., Barber, N., and Bradley, C. P. (2000), "Doctor-patient communication about drugs: The evidence for shared decision making," *Social Science & Medicine*, 50, 829–840.

Stewart III, C. and Woon, J. (2017), "Congressional Committee Assignments, 103rd to 114th Congresses, 1993–2017: House and Senate, updated to August 18, 2016," .

Stremersch, S., Landsman, V., Venkataraman, S., and Stremersch, S. (2013), "The Relationship Between DTCA, Drug Requests, and Prescriptions: Uncovering Variation in Specialty and Space," *Marketing Science*, 32, 89–110.

Surroca, J., Tribo, J. A., and Waddock, S. (2010), "Corporate Responsibility and Financial Performance: The Role of Intangible Resources," *Strategic Management Journal*, 31, 463–490.

Toole, A. A. (2007), "Does Public Scientific Research Complement Private Investment in Research and Development in the Pharmaceutical Industry?" *The Journal of Law and Economics*, 50, 81–104.

Trouiller, P., Olliaro, P., Torreele, E., Orbinski, J., Laing, R., and Ford, N. (2002), "Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure," *The Lancet*, 359, 2188–2194.

Venkataraman, S. and Stremersch, S. (2007), "The Debate on Influencing Doctors' Decisions: Are Drug Characteristics the Missing Link?" *Management Science*, 53, 1688–1701.

Werner, T. (2015), "Gaining Access by Doing Good: The Effect of Sociopolitical Reputation on Firm Participation in Public Policy Making," *Management Science*, 61, 1989–2011.

World Health Organization (2016), "Glossary," .

Yamey, G., Thoumi, A., Gonzalez-Smith, J., Binanay, C., Bharali, I., Johar, Z., Ridley, D., and Chapman, N. (2017), "Strengthening the United States Government's Role in Product Development for Global Health," .

Zgierska, A., Miller, M., and Rabago, D. (2012), “Patient Satisfaction, Prescription Drug Abuse, and Potential Unintended Consequences,” *JAMA*, 307, 1377–1378.

Biography

Su Zhang was born in Jishou, China on September 18, 1988. He attended Huazhong University of Science and Technology from 2006 to 2010, where he received a B.A. in Economics. He started his study in the economics graduate program at Duke University in 2010. He earned his Masters in Economics in 2012 and his Ph.D. in Economics in 2018 from Duke University. As a graduate student, he specialized in empirical Industrial Organization. Su will join Analysis Group as an associate in the summer of 2018.