Marketing Regulation, Social Contagion, and the Diffusion of Stimulant, Antidepressant, and Antipsychotic Medications

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ABSTRACT

The pharmaceutical industry spends roughly 15 billion dollars each year on detailing – providing gifts, samples, free pens, trips, honoraria and other inducements to physicians in order to encourage them to prescribe their drugs. In response, a movement to regulate pharmaceutical marketing emerged. In this article, we use a dataset that captures 60 percent of prescriptions written in the United States to examine how marketing regulation, peer influence, and drug characteristics shaped the diffusion of four new medications. We show that regulation of pharmaceutical marketing significantly reduces physicians’ propensity to prescribe newly marketed medications. Moreover, in states that ban gift-giving or require disclosure of marketing gifts and payments, peer networks substitute for pharmaceutical detailing when an innovative drug comes to market. This indirect effect of regulation allows for the diffusion of information about new drugs through channels that are less subject to conflicts of interest. Our analysis augments the literature on the diffusion of innovations by showing that the extent to which products diffuse, as well as the pathways through which diffusion occurs are influenced by how innovative a product is and regulatory context. It also adds to a growing body of work on market transformation by considering indirect effects of information-based regulation.
Pharmaceutical companies invest heavily in marketing. Between 1990 and 2008, pharmaceutical expenditures on marketing increased nearly six-fold from $3 billion dollars to more than $20.5 billion dollars (Congressional Budget Office, 2009). A practice commonly known as detailing, in which drug company representatives make sales calls to physicians and provide them with information, free samples, literature, and gifts, accounted for the majority of promotional expenses. Collectively, pharmaceutical companies spent $15.7 billion dollars on detailing in 2011 or roughly $19,000 for every physician in the United States (Kaiser Family Foundation, 2013, Pew Charitable Trusts, 2013). The majority of studies examining pharmaceutical marketing find that detailing has small but significant effects on drug uptake and utilization (For reviews see Stremersch et al. 2008; Manchanda and Honka 2005; Kremer et al. 2008). One suspects that the effects are more pronounced than these studies reveal: after all, why would the pharmaceutical industry spend 15 billion dollars annually if they believed the impact was so limited.

This belief has led to increased public and regulatory scrutiny of pharmaceutical detailing. By creating situations in which a physician’s professional judgment may be at odds with his or her own personal self-interest, detailing may lead to conflicts of interest. Amidst growing concern about potential conflicts of interest in medicine generated by detailing, a host of states, medical schools, and interest groups have begun to advocate for policies to regulate interactions between physicians and pharmaceutical representatives.

Efforts to transform the pharmaceutical industry have taken a variety of forms ranging from self-regulation to laws prohibiting physicians from receiving gifts from pharmaceutical companies. In 2002, medical students began taking PharmaFree pledges, promising “to accept no money, gifts, or

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1 Detailing expenditures exclude drug samples which account for an additional $6.2 billion. Calculating pharmaceutical marketing expenditures is notoriously difficult since companies do not disclose what they spend on marketing. For instance, estimates for 2004 ranged from $27.7 billion to $57.5 billion. Comparatively, pharmaceutical companies spent $31.5 billion on research and development in the same year (Gagnon and Lexchin 2008). The estimate reported here uses data that produces lower bound estimates.
hospitality from the pharmaceutical industry.” The American Medical Association, the American College of Physicians, as well as the Pharmaceutical Research and Manufacturers Association have all established quasi-voluntary codes of conduct to self-regulate physician-industry collaborations. Academic medical centers have implemented policies to govern interactions between students and faculty and pharmaceutical company representatives. By 2009, eight states had adopted laws regulating interactions between pharmaceutical representatives and physicians. Finally, the Physician Payment Sunshine Act, required all drug manufactures to publicly disclose financial relationships with physicians beginning in 2014.

Despite the growing movement for pharmaceutical marketing reform, little is known about whether policies governing physician-industry interactions have affected the market for pharmaceuticals. In this article, we use a dataset that captures 189 million antidepressant, antipsychotic and stimulant prescriptions written in the United States to examine how regulation impacted the diffusion for four newly introduced medications. In doing so, we contribute to research on regulation, innovation, and market transformation by comparing how different regulatory forms—self-regulation and disclosure versus command and control style regulation—shaped the diffusion of innovations. Differences in regulatory type and strength allow us to disentangle the multiple pathways by which information about new drugs diffused. For instance, bans on gift-giving enable us to assess the importance of gifts for new drug uptake. We further consider the indirect effects of different regulatory forms by examining whether regulations targeted at pharmaceutical companies change communication patterns among physicians.

Moreover, we analyze whether the pathways by which drugs diffuse differ depending on characteristics of the drug itself—its innovativeness. We thereby address two issues that remain under investigated in the literature on the diffusion of innovations. First, relatively few studies
examine how characteristics of the innovations affect patterns and pathways of diffusion (Wejnert, 2002, Rogers, 2003, Rossman, 2012a). In addition, little is known about when and why certain pathways of diffusion take precedence over others (Strang and Soule 1998; Rossman 2012).

To preview our main findings, marketing regulation has a substantial and significant impact on physician prescribing behavior. The extent to which products diffuse, as well as the pathways through which diffusion occurs are influenced by both how innovative a drug is and regulatory context. In states that ban gift-giving and require disclosure, peer networks substitute for pharmaceutical detailing when an innovative drug comes to market. This indirect effect of regulation allows for the diffusion of information about new drugs through channels that are less subject to conflicts of interest. This has important implications for research on regulation, diffusion, and market transformation.

Forms of Regulation and Market Transformation

A large body of work has documented how public policies and regulations can transform markets (Dobbin and Dowd, 1997, Fligstein, 2003, Sine and Lee, 2009). Scholars have also shown how non-state actors, particularly social movements, transform markets by directly targeting firms (King and Soule, 2007, Weber, Rao, and Thomas, 2009, King and Pearce, 2010), by influencing state regulatory policy (Ingram and Rao 2004; Schneiberg and Bartley 2001), promulgating new organizational forms (Schneiberg, King, and Smith 2008), and by creating and legitimating new markets (Klaus Weber, Heinze, & DeSoucey, 2008, Hiatt, Sine, & Tolbert, 2009). Efforts to reform corporations and markets have also yielded a variety of private regulatory instruments including self-regulation, regulation by information, certification systems and other types of soft-laws (Bartley, 2003a, 2007, Vogel, 2008b). While the existing literature has documented how and why new regulatory forms
emerge and diffuse, less work has examined how these new regulatory forms shape outcomes (Schneiberg and Bartley 2008; Short and Toffel 2010).

Self-regulation is a form of soft regulation in which private firms or interest groups commit to modifying their own behavior and often assume regulatory responsibilities traditionally performed by the state, such as standard setting, developing codes of conduct, disclosure, and certification. These programs can be put into place with state support and oversight (Short and Toffel, 2010) or independent of the state. There is increasing consensus within the literature that the success and failure of these policies is contingent (King and Lenox, 2000, Bartley, 2003, Darnall and Sides, 2008, Innes and Sam, 2008, Yue, Luo, and Ingram, 2013, Perkmann et al., 2013). Successful self-regulation is most likely to occur when the behavior of corporations is visible to outside monitors and explicit sanctions exist for violations (King and Lenox 2000; Short 2013; Short and Toffel 2010). In cases of successful self-regulation, the state often serves as a monitor and enforcer (Short and Toffel 2010; Short 2013). In highlighting the contextual nature of successful implementation of softer-forms of regulation, such as information based regulation, self-regulation, and certification, scholars have started to ask not just whether or not policies work but how they work.

Work in social psychology has found that information-based regulation, such as mandatory gift reporting and other forms of disclosure, are unlikely to reduce biases generated by gift-exchange and similar practices since the psychological biases generated by accepting gifts are not deliberate choices (Dana & Loewenstein, 2003). The biases are unconscious and unintentional. As write Dana and Loewenstein (2003:254) write, “A research-informed understanding of conflict of interest has important implications for policy. Specifically, the interventions mentioned earlier—limiting gift size, educational initiatives, and mandatory disclosure—are unlikely to eliminate bias because they rest of
a faulty model of human behavior” (Dana and Loewenstein, 2003:254). From this perspective, information based regulation is unlikely to have a discernible effect on physician prescribing behavior. Moreover, disclosure may not only be ineffective, it may lead to perverse consequences by diminishing guilt and providing moral license (Cain, Loewenstein, and Moore, 2005). Instead of disclosure and soft gift limits, scholars have proposed education and cultural changes (Sah and Fugh-Berman, 2013) and gift bans (Dana and Loewenstein, 2003) as preferable remedies. Thus, it is not immediately obvious what effect--if any--regulations requiring disclosure of payments and gifts or placing soft limits on dollar amounts will have on physician prescribing behavior.

Relatively little attention has been devoted to indirect effects of information-based regulation. However, within the literature on organizational behavior it has been widely documented that changes in legal environments can have indirect consequences that extend well beyond the letter of the law (Edelman, 1990, Edelman and Suchman, 1997). Similarly, the literature on social movements and corporate reform has found that movements often have indirect and sometimes unanticipated consequences (Haveman, Rao, and Paruchuri 2007; Hiatt et al. 2009; Schneiberg et al. 2008). Since self-regulation and other types soft-regulation lie along a continuum with bottom-up collective action at one end and top-down state-based regulation at the other (Vogel, 2008a), we anticipate that these regulatory forms will also have indirect effects and unanticipated consequences. These indirect effects could have important implications for understanding the effectiveness of newer regulatory forms and their ability to shape patterns of diffusion. Recent work by Schneiberg (2013) demonstrated that social movements can serve as political conditions for diffusion suggesting that efforts to reform pharmaceutical marketing will likely impact new drug diffusion. In this study we examine how regulatory policies arising from movements to reform pharmaceutical marketing
practices directly and indirectly shaped the patterns and pathways of diffusion of four new medications.

*Diffusion, Regulation, and Market Transformation*

A long history of sociological inquiry has focused on the diffusion of innovations and much of it has centered on the diffusion of medical innovations. Since Coleman, Katz, and Menzel’s (1966) seminal work, *Medical Innovation*, which examined the diffusion of a new medication, scholars have been interested in the role of peer effects in the diffusion of innovations. A large body of research has documented numerous pathways through which diffusion occurs and attempted disentangle whether endogenous (e.g., social influence and peer-to-peer information sharing) or exogenous processes (e.g., broadcast media and change agents) account for the observed patterns of diffusion. Many of the debates over the role these pathways play in diffusion have been played out in reanalyses of Coleman, Katz, and Menzel’s original data (Burt, 1987, Strang and Tuma, 1993, Van den Bulte and Lilien, 2001). While progress has been made in identifying various paths of diffusion, little is known about how characteristics of innovations influence the rate at which and pathways by which innovations spreads (Rossman 2012).

The dearth of research examining how product characteristics relate to rates and pathways of diffusion may arise from a general bias within the literate towards ideas and products that are truly innovative and/or successfully diffuse (Soule 1999; Strang and Soule 1998), as well as methodological and data limitations which have typically limited the number of innovations examined in any single study (Rossman 2012). In order to understand how novelty and innovativeness- key characteristics in the spread of innovations- shape rates and patterns of diffusion.

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While there are large literatures on the diffusion of ideas, practices, and principles we largely confine our discussion to the literature pertaining to product diffusion.
diffusion, studies must examine the diffusion of products, tactics, or ideas that are both successful and unsuccessful (Soule, 1999, Wang and Soule, 2012). With respect to the pharmaceutical context, research by Venkataraman and Stremersch (2007) began to address these issues and found that physicians’ responses to marketing efforts were moderated by drug effectiveness and side effects. However, the extent to which product novelty affects pathways of diffusion, thereby shaping overall patterns of diffusion remains unknown.

State-level differences in regulatory strength allow us to begin to trace the multiple pathways by which information about new drugs diffused and assess whether certain pathways of diffusion were more or less active for innovative medications. Recent studies have found that physicians exposed to conflict of interest policies during medical training are less likely to prescribe newly marketed psychotropic medications over older cheaper alternatives (King et al., 2013) and are more likely to prescribe generic medications (Epstein et al., 2013). These findings suggest that in the absence of conflict of interest policies physician prescribing behavior is influenced by pharmaceutical detailing and gift giving. However, neither study analyzes how drug characteristics influence physicians’ adoption and prescribing patterns once regulation is implemented. Moreover, neither of these studies examine whether alternative pathways of diffusion exist as possible substitutes for pharmaceutical detailing.

Policies aiming to reduce conflict of interests by limiting detailing could lead to unanticipated negative consequences if physicians do not have alternative sources of information about innovative new medications. Of central interest, then, is whether regulation can catalyze the activation of physician networks. These networks can then serve as an alternative pathway for information to diffuse. When an innovative drug comes to market in a state limiting pharmaceutical detailing, will doctors learn about it from other doctors? Or will the new innovative drug go unnoticed? In the
following pages, we address these questions by examining the effect of pharmaceutical marketing regulation on the diffusion of newly introduced antidepressant, stimulant, and antipsychotic medications.

*Pharmaceutical Marketing Regulation*

Over the past decade, physician-industry interactions have come under increased state and federal oversight. Previously, the American Medical Association (AMA) and the Pharmaceutical Research and Manufactures of American (PhrMA) had developed quasi-voluntary guidelines and codes of conduct. In order to avoid state regulation, these organizations ensured that self-regulation was the primary means of regulating physician-industry interactions. While both organizations developed suggested guidelines for what types of physician-industry interactions and gifts were appropriate, neither organization developed mechanisms for compliance or enforcement nor did they require disclosure of payments and gifts. Dissatisfied with industry efforts to self-regulate, numerous states have adopted policies to govern interactions between representatives of pharmaceutical manufacturers and physicians or made industry based guidelines part of state regulatory efforts (Rodwin, 2011).

By 2009, eight states had adopted laws regulating pharmaceutical marketing. These laws varied in regulatory strength but collectively encompass three areas: (1) requirements that manufacturers disclose payments and gifts to physicians, (2) prohibitions banning certain gifts, and (3) mandates that pharmaceutical companies comply with the code of conduct and guidelines originally developed by the Pharmaceutical Research and Manufactures of America (Gorlach and Pham-Kanter, 2013a).
Vermont, Massachusetts and Minnesota have the most comprehensive disclosure requirements and gift bans. All three states directly prohibit many gifts by law. Minnesota introduced the first state-level regulation governing interactions between physicians and pharmaceutical representatives in 1993. The legislation, which remains among the most stringent in the United States, banned gifts totaling $50 or more in a given year from a single company and created mandatory reporting of all honoraria, consulting, and other payments benefiting the physician that are not classified as gifts. Similar legislation requiring mandatory reporting of payments exceeding $25 was enacted by Vermont in 2002. This legislation was subsequently strengthened to include a ban on all gifts, including food, to health care professionals that went into effect in 2009. In 2009, Massachusetts implemented regulation restricting payments and gifts and establishing a mandatory reporting requirement. Disclosure data from Vermont, Minnesota, and Massachusetts is publicly available and identifies individual physicians.

Four additional states and the District of Columbia have enacted legislation regulating pharmaceutical marketing. However, these regulations are less comprehensive than the policies enacted in Vermont, Massachusetts, and Minnesota. Three states—Maine (2003), West Virginia (2004), and Washington D.C. (2004)—require pharmaceutical companies to report aggregated marketing expenditures to the state, but these reports are not made public. California, Nevada, and Washington DC mandate that pharmaceutical companies adopt codes of conduct, develop internal

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3 In both Vermont and Minnesota there are exemptions for expenditures that are not considered “gifts,” including honoraria, consulting payments, samples, and educational materials.

4 While payment data in these three states is publicly available, the ease of access and quality of the data varies. See Ross et al. 2007 for a summary of Vermont and Minnesota’s data. Massachusetts, which implemented in 2009, is still in the process of developing a mechanism to make payment data available.
compliance mechanisms, and file annual reports documenting compliance yearly. As part of the code of conduct in California, companies must develop specific annual dollar limits on gifts and promotional items given by the manufacturer to health care providers. In California, Nevada, and DC state statues are largely based on the guidelines developed by the Pharmaceutical Research and Manufactures of America (National Conference of State Legislatures, 2013, Gorlach and Pham-Kanter, 2013b).

To examine how regulatory environments shaped diffusion processes, we classified states by the strength of their regulation: Vermont and Minnesota are coded as “strict” regulatory regimes because the states directly limit gifts to physicians and make payment data at the individual physician level publically available. This creates incentives not only for pharmaceutical companies to change their behavior, but incentivizes doctors as well. Maine, West Virginia, California, Nevada, and Washington D.C. are coded as having “weak regulation.” While these states varied in the strength of their regulation, there is a clear qualitative difference between states that explicitly prohibit or limit gifts and have public accountability mechanisms and those that do not. All other states are classified as having no pharmaceutical regulation. Since Massachusetts adopted regulation after the study period, it is included in the set of states with “no policy.” To examine the impact that regulation has on physician prescribing patterns, we examined physicians’ propensity to prescribe newly introduced and marketed mental health medications.

*Mental Health Medications*

Mental health medications are currently among the best selling and most heavily marketed classes of drugs in the United States. One in five adults in the United States received a mental health medication in 2010. In that year, sales of antidepressant, antipsychotic, and stimulant medications yielded close to $35 billion dollars and accounted for 11.4% of total U.S. spending on
pharmaceuticals (IMS Incorporated 2010). Stimulants, antidepressants, and antipsychotics are also among the top five most heavily detailed drug classes (Congressional Budget Office, 2009). Given the importance of these classes of medications to the pharmaceutical industry, our study focuses on four newly introduced mental health medications.

Newly introduced drugs are substantially more expensive than the older alternatives and have contributed to both rising health care costs, as well as pharmaceutical revenues. The shift to newly introduced and heavily marketed medications accounted for 36% of the rise in all retail drug spending in 2000 and 24% of the increase the following year, the last year data was available (National Institute for Health Care Management 2002). Compared to other classes, the increased tendency of physicians to prescribe newly introduced mental health medications has disproportionately greater cost implications (Duggan 2005).

Our analysis focuses on four medications introduced within these classes during our study period: Vyvanse (stimulant), Invega (antipsychotic), Pristiq (antidepressant) and Cymbalta (antidepressant). Cymbalta was introduced four months prior to the beginning of our dataset; all other medications were introduced during the study window. No other oral mental health medications were introduced during the study period. These medications are ideally suited to studying new drug diffusion since they vary in how innovative they are relative to existing alternative medications within the class.

The FDA simply requires medications to be more efficacious than a placebo. It does not mandate that companies compare the effectiveness of a newly introduced drug to existing alternatives in what are known as head-to-head drug trials. Since head-to-head trials are rarely conducted, determining how innovative a new medication is necessitates compiling published and unpublished studies and clinical trials for all existing drugs in the class to assess relative drug efficacy, adverse events, and side

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5 Drug companies often selectively report results of clinical trials and follow-up studies so it is important to examine unpublished studies to the extent possible.
effects. In an effort to provide unbiased information on available medications to healthcare professionals, *The Medical Letter on Drugs and Therapeutics* (commonly known as the Medical Letter) was established in 1959.

The *Medical Letter* is a non-profit publication solely supported by subscription (it does not accept grants, donations, or funding from outside entities) and is thus free from many of the obvious conflicts of interest that are common in the pharmaceutical industry. In reviewing new drugs and developing treatment guidelines, an expert reviewer at the *Medical Letter* first develops a preliminary draft describing medications in terms of their efficacy, side-effects, adverse effects, and compares them to existing alternatives. The preliminary draft is then circulated to all members of the advisory board, 10 to 20 researchers with relevant clinical or experimental expertise in the area, first authors of all of the clinical trials referenced, drug manufacturers as well as to the FDA and the Centers for Disease Control. Comments from these parties are then reviewed and incorporated into the final draft as appropriate. Describing the editorial process of the *Medical Letter* and its importance to the medical field, Dr. Zuccotti, deputy editor at the New England Journal of Medicine wrote, "The unique editorial process used to produce Treatment Guidelines results in prescribing recommendations that are free of pharmaceutical influence" and produces “trusted recommendations.” Given the importance and standing of the *Medical Letter* within the field of medicine, we will draw heavily on the journal’s reports in typifying medications according to their innovativeness. While the drugs examined in this study vary in their level of innovation, none are radical breakthroughs in their class and all relied on active ingredients already available on the market. Of the medications examined in this study Vyvanse and Cymbalta had the most advantages over existing medications within their respective classes.
Vyvanse. Vyvanse is a stimulant used to treat attention-deficit/hyperactivity disorder. While Vyvanse relies on active ingredients that are already available on the market, the process by which it is metabolized makes it less prone for abuse and longer-lasting. The reduced potential for abuse is an important development within the class since stimulants are among the most commonly misused prescription medications (NIDA 2012). The Medical Letter described Vyvanse stating, it “has no euphoric effects if given IV [intravenously] or taken intranasally and is thought to have less potential for abuse than amphetamine itself. The duration of action of lisdexamfetamine (Vyvanse) is longer than that of other amphetamine preparations, which may be an advantage for use in working adults.”

Cymbalta. Cymbalta (duloxetine) is a serotonin and norepinephrine reuptake inhibitor (SNRI) approved to treat major depressive disorder in August of 2004. A month later it received an additional indication for treating pain associated with nerve damage due to diabetes. In marketing Cymbalta, Eli Lilly emphasized the medication’s indication for pain and its possible utility for treating the physical symptoms of depression. In June 2008, Cymbalta was approved for treatment of Fibromyalgia. During the study period, only two medications were approved for treating Fibromyalgia which affects two to four percent of the population. Describing Cymbalta’s utility for treating Fibromyalgia, The Medical Letter wrote it “appears to be effective in reducing the symptoms of Fibromyalgia” and “has the advantage of once-daily dosing and possibly adding effective treatment for depression, which is common in patients with fibromyalgia.” (Medical Letter July 28, 2008). Cymbalta was subsequently approved to treat chronic low back pain and osteoarthritis in 2010, providing additional evidence that the medication is effective in treating pain alongside depression, though the mechanism by which it does so remains unknown.

6 In 2010, it is estimated that 1.1 million Americans abused stimulants.
Pristiq and Invega. While Cymbalta and Vyvanse have advantages over existing alternatives within their respective classes, Pristiq and Invega are structurally similar to existing medications and offer little or no known advantages. Both Pristiq and Invega are partially metabolized products of an existing drug. When a patient takes Invega, their body automatically converts it into risperidone which is already generically available. Similarly, Pristiq is automatically transformed into Effexor. As a result, Pristiq was described in the Medical Letter as having “no demonstrated clinical advantage over the parent compound.” Similarly, Invega was found “to be similar to risperidone in effectiveness and adverse effects...[with]...No specific advantages.” Wyeth withdrew its application for marketing authorization for Pristiq in the European Union after concerns were expressed over its lack of efficacy and similarity to Effexor. Pristiq is not approved for use in the E.U.

As Table 2 summarizes, there were considerable differences in the innovativeness of the four drugs introduced during the study period. Vyvanse had less potential for abuse than other medications on the market and was also marketable to adults because of its long-lasting formulation. Cymbalta with a pain indication had a point of differentiation that was heavily marketed to gain market share in the crowded antidepressant space. In contrast, both Pristiq and Invega offered no improvement over existing medications. The variation in the innovativeness of these drugs provides an opportunity to examine whether the affect of marketing regulation varies by the characteristics of the medication.

Data and Methods

Data for this study came from IMS LifeLink™ LRx Longitudinal Prescription database, which contains de-identified individual prescriptions from approximately 33,000 retail pharmacies, food
stores, independent pharmacies, as well as mass retailers. Over 60% of all retail prescriptions in the United States are covered in the LRx database. During the analysis period, coverage of the total LRx database ranged from 224,140,604 unique individuals who filled at least one prescription for any medication at the beginning of the study period to 233,592,728 individuals at the end of the study period.

The subset of the data we focus on covers 47,607,531 patients who received at least one prescription for an antidepressant, stimulant, or antipsychotic medication between January 1, 2005 and April 30, 2009. Of central interest is the prescribing behavior of the 916,338 physicians who wrote at least one prescription for an antidepressant, antipsychotic, or stimulant to one of these patients. The dataset captures at least one prescription for 80% (916,338/1,144,790) of physicians in the United States. The data is geographically representative and is representative by sex, age, and insurance coverage and has been used in numerous publications within the medical literature (for examples see Jackevicius et al. 2011; King et al. 2013).

Each prescription in the LRx database contains a unique patient identification number, prescriber identification number, the patients’ sex, year of birth, whether the prescription was paid for by Cash, Medicaid or Third Party insurance, the date the prescription was dispensed, and the medication the prescription was written for. Using an encrypted prescriber identification number, it is possible to link the prescription to information about the physician including the three-digit zip code in which the physician practiced, their specialty, the year they graduated medical school, the medical school from which they received their degree, as well as the physicians’ date of birth and sex. Both the physician and the patient can be tracked longitudinally using their unique identification number. We exploit all of these data in the analysis below. All analyses are conducted by class with physician-

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7 Interestingly, four out of five physicians—regardless of specialty—prescribed an antidepressant, antipsychotic or stimulant during our study period.
month as the unit of analysis. Physicians were considered eligible to prescribe a newly introduced medication and were thus included in our analysis if they prescribed at least one medication within the class of interest during the analysis period. For instance, a physician would be included in the Vyvanse analysis if she prescribed at least one stimulant, regardless of what medication the prescription was written for. Physicians are only included in the analysis when they have written at least one prescription during the focal month.

**Analysis Strategy**

The first goal of our analysis was to determine whether patterns of diffusion differed by drug across the three regulatory environments. In particular, we were interested in whether regulatory effects and drug penetration varied by the innovativeness of the medication. To examine overall patterns of new drug penetration, we plotted the mean number of prescriptions written for each drug by month. Plots were constructed for states with strict, weak, and no pharmaceutical regulation by month. Given our interest in how regulation affects prescribing levels of newly introduced mental health medications, our focus is on the prescribing rate of new medications. The longitudinal span of the dataset allows us to examine prescribing patterns over time and does not limit us to looking at time to first adoption. While the literature on diffusion often focuses on time to first adoption, the level of prescribing is more interesting for our analysis given our goal of understanding factors undergirding the growing mental health medication market and the possible policy implications of the analysis.

After examining prescribing rates by regulatory regime, we then model physician prescribing rates to estimate regulatory effects. For Cymbalta and Vyvanse we estimated negative binomial models with state level random-effects (Cameron and Trivedi 1986), in which the dependent variable in all
analyses was the number of prescriptions written for a newly introduced medication in a month by a physician practicing in a given state. The total volume of prescriptions written by physicians in that class was used as the exposure variable in these models. Invega and Pristiq were modeled using random effects logit models since, 97.1% and 96.4% of doctors in a given month wrote one or fewer prescriptions for these drugs, respectively. All models are restricted to the first year the medication of interest is on the market. Separate models were estimated for Vyvanse, Cymbalta, Invega, and Pristiq, which allowed us to quantify the size of regulatory effects for each of the four newly introduced medications.

To examine the effects of pharmaceutical regulation on physician prescribing patterns, we included dummy variables for policy strength—strong, weak, or no policy—using no policy as the reference category in our models. Based on the existing literature, we also included several physician characteristics as control variables: physician specialty, year of graduation from medical school, and insurance composition of physicians’ patients. Physician specialty dummies were created for each analysis based on the dominant specialties prescribing within each class of medication based on volume. Since there is considerable variability in principal prescribing specialties across the classes of medications, the specialty dummies vary across the different medications. The insurance composition of the physicians’ patients was characterized by the percent of patients with third-party insurance, which includes Medicare, percent paying with cash, and percent of patients covered by Medicaid. The largest category, percent of patients with insurance, was used as the reference category. Within class prescribing volume is either included as a control or exposure variable depending on the type of model being estimated. Finally, all models included the physician’s lagged prescription volume of the focal drug. This is not dichotomized in models for Pristiq and Invega. Incorporating the lagged prescribing volume of the drug of interest helps eliminate autocorrelation and takes into account that prescribing volumes at $t+1$ are likely a function of prescribing at time $t$. 
After establishing that prescribing patterns vary significantly across regulatory environments, we wanted to gain a better understanding of the pathways that might account for differences in prescribing rates across regimes. To do so, we examine the relative importance of marketing and peer effects. Of particular interest was whether the strength of peer effects varied across regulatory environments. We anticipated that peer effects would be stronger for newly introduced medications that offered a recognizable improvement over existing alternatives than for less innovative medications. Moreover, peer effects should be stronger in states with strict marketing regulation since information from peers would be more important in environments in which marketers have less of an opportunity to act as an alternative source of information.

To examine the importance of peer influence for each of the medications, we included the lagged prescribing volume of physicians who practice in the same three-digit zip code, attended the same medical school, graduated in the same year, and are of the same specialty as the focal physician. In 2008, the average size of the graduating medical school class was 128 students, though this varied considerably by school from a low of 24 to a high of 308. To ensure that physicians would have known or at least encountered each other in medical school, we restricted our analysis to physicians graduating from the same school in the same year. To further increase the likelihood that they would be in contact in the current periods, we restricted to physicians of the same specialty, practicing in the same three-digit zip code. This was the most restrictive definition of “peer” available given our data structure, but also had seems reasonable given the size of medical schools and the nature of medical practice. Of physicians who prescribed an antidepressant during Cymbalta’s time on the market 6.6% (56,673/850,968) had at least one peer by this definition and 9.4% (60,930/650,204) had a peer during Pristiq’s time on the market. Peers could be identified for
10.2% (39,038/381,246) of physicians prescribing a stimulant after Vyvanse’s introduction and 8.7% (34,966/403,438) of physicians who prescribed an antipsychotic after Invega’s introduction.

Previous research has demonstrated that peer effects can be cofounded by marketing effects. Accordingly, it is important to control for marketing efforts when estimating peer influence (Van den Bulte and Lilien, 2001, Nair, Manchanda, and Bhatia, 2010). Regulatory regimes, which are central to our analysis, help us assess whether or not peer effects are being confounded by marketing efforts in our analyses. If, as we hypothesize, peer effects are most important in areas that limit pharmaceutical marketing, we should see stronger peer effects when marketing efforts are limited. If we only observe peer effect effects in states that limit pharmaceutical marketing, it is unlikely that our measure of peer influence is simply capturing marketing efforts. Moreover, the lagged dependent variable in our analysis acts as a control for physician directed marketing efforts since pharmaceutical companies allocate detailing efforts primarily based on previous physician prescribing patterns.

To assess whether the importance of peer influence varied by regulatory environment, we included interactions between the policy variables and lagged volume of peer prescribing of the focal drug. Collectively, these series of analysis allow us to examine the patterns and pathways of diffusion for four newly introduced medications in different regulatory regimes. To examine how peer influence changes over time and across different regulatory environments we estimated models two sets of models. The first set of models examine physician prescribing in the first year a medication is introduced. In order to assess whether peer effects are stronger shortly after a drug is introduced, we conducted a second series of analyses that are restricted to the first four months after introduction. Given how rarely physicians in certain regulatory environments prescribed Invega and Pristiq, it was
necessary to conduct analyses examining only the first four months of prescribing by comparing prescribing rates in areas with any type of marketing regulation to areas without regulation. It was not possible to examine peer influence by the strength of regulation (strict versus weak) for these medications. There simply were not enough physicians prescribing these medications to estimate models without a greater level of aggregation. For instance, in Minnesota and Vermont, states with strict marketing regulation, Invega was only prescribed 15 times in its first month of introduction. For Vyvanse and Cymbalta, which had a higher market penetration, it was possible to estimate models for the first four months of prescribing with more refined measures of regulatory strength. We anticipate that the importance of peer effects will diminish over time as knowledge about the new drug has diffused.

After examining temporal variation in responses to regulation, we graph the predicted number of prescriptions written for each medication in an average month during the first year the product was on the market. Using the margins command in Stata, we generated predicted prescribing rates by policy regime based on estimates from the baseline models. In order to examine the importance of peer effects in each regulatory regime, we estimated predicted prescribing rates by regulatory regime with no peer prescribing of the focal drug and peer prescribing at one standard deviation above the mean.

Sensitivity Analyses
To assess the adequacy of lagged prescribing volume of the drug of interest as a proxy for pharmaceutical marketing efforts, we conducted several sensitivity analyses. First, we obtained pharmaceutical marketing expenditures within three-digit zip codes for Johnson and Johnson (2013), Eli Lilly (2013), and Pfizer (2010). Cymbalta is manufactured by Eli Lilly, Invega is produced by
Johnson and Johnson and Pfizer manufactures Pristiq. All three companies began disclosing data on gifts and payments to physicians as part of settlements with the U.S. Justice Department over illegal promotional practices. While manufacturers do not disclose which drugs the payments or gifts are associated with, Cymbalta was the most heavily marketed Lilly medication and Pristiq had the largest expenditures among Pfizer drugs in Vermont which releases drug-specific payments. Among all medications in all classes, Cymbalta, Pristiq, and Vyvanse ranked first, third, and eighth in overall marketing expenditures respectively. Thus, it is reasonable to expect that total marketing expenditures capture detailing for the drugs of interest. Data for the manufacturer of Vyvanse (Shire) was not available, so we use data on expenditures by other manufactures in our analysis that produce ADHD medications.

We acquired the earliest payment reports available for each company. Due to restrictions on data availability, the payment data used in our analysis captures gifts and payments made outside of our study window. An analysis of serial dependence in physician payments by geographic area found that geographic distribution of payments across two years had a correlation of 0.99, p<0.001 (King and Essick 2013), which assuaged our concerns about using payment data that was collected outside of our analysis period. We geocoded physician payment data and then aggregated payments to the three-digit zip code. To get a measure of average expenditures per physician in the three digit zip code, we divided the total amount spent on marketing by the number of physicians in the area. This allowed us to incorporate area level variation in pharmaceutical marketing in our model. In addition, we estimated models with zip code fixed effects to assess whether our estimates of peer effects, which partially rely on co-location, could be capturing joint exposure to a successful detailer or practicing in an elevated marketing territory. Models that included zip code fixed effects were

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stratified by regulatory environment. Collectively, these analyses allowed us to assess the robustness of our results to area level variation in marketing.

One of the benefits of incorporating lagged prescribing volume in our models is that it allows us to control for targeting bias that might arise from detailers targeting individual physicians with a history of prescribing the focal drug. We also estimated models that included physician fixed effects instead of a lagged dependent variables to assess whether our results could arise from detailers targeting physicians who have a higher unobserved probability to prescribe the focal medication due to time invariant characteristics, such as prior training or stable preferences, not captured in our models.

More generally, attempts to identify and estimate peer effects must deal with three problems discussed extensively in the literature: simultaneity, correlated unobservables, and endogenous group formation. Our use of physician fixed effects, zip code fixed effects, and lagged dependent variables help address these issues. Correlated unobservables at either the individual or community level could lead physicians and their peers to simultaneously adopt a drug, not as a result of peer influence, but due to similarities not captured in our data. This would produce a spurious correlation that could be mistaken for a peer effect. Unobserved individual characteristics, such as preferences, training, or practice style, common to both the physician and their peers could also produce biased estimates of peer effects. Models including physician fixed-effects and zip code level fixed effects help overcome these issues. Finally, our concerns about simultaneity are mitigated by using peers’ lagged prescribing volume.
Results

Patterns of diffusion varied considerably by drug characteristic and regulatory environment. As shown in Figure 1, prescribing rates for all newly introduced medications were highest in states with no marketing regulation and lower in states with marketing regulation. There were also considerable differences in the size of the regulatory differences across the four medications. In absolute terms, the differences across regulatory regimes were the greatest for Vyvanse. However, relative differences in prescribing across regulatory regime were greatest for Pristiq and the weakest for Cymbalta. These differences are summarized in the descriptive statistics in Appendix A.

Turning to the models examining regulatory strength and prescribing rates, we find further evidence that prescribing rates vary by regulatory environment after controlling for physician level characteristics. In all four base-line models both policy variables were statistically significant at p<0.001. Moreover, pharmaceutical regulation substantially reduced prescribing rates of newly marketed medications. All medications saw a more than 25% reduction in prescribing when marketing regulations were in place. Prescribing of Vyvanse was 43% lower in strict regulatory regimes and 45% lower in areas with weaker regulation than in areas without regulation. Invega prescribing was 34% and 35% lower in strict and weak regulatory regimes, respectively. Surprising, the strength of marketing regulations had little impact on physician prescribing rates—the primary difference was between states with no marketing regulation and states with any form of regulation. Large differences in regulatory strength were only observed for Pristiq. In areas with stringent marketing regulation, prescribing was reduced by 73% whereas in areas with more limited restrictions prescribing declined 33%.
After establishing that physicians’ propensity to prescribe newly introduced medications varied by regulatory environment, we wanted to examine whether peer effects were stronger when marketing influences were limited by regulation. This is particularly important for innovative drugs that offer an advantage over existing medications since alternative pathways of diffusion of information about new drugs would be critical in these environments. There was a positive association between a physician’s prescribing rate of Vyvanse and Cymbalta and the prescribing rate of his or her peers, which was particularly strong in states with marketing regulation. The event rate ratio for peer effects for Cymbalta was 1.11 (95% CI: 1.08, 1.14) in areas with strict marketing regulation and 1.03 (95% CI: 1.01, 1.04) in areas with weak marketing regulation during the first year the medication was on the market. For Vyvanse, we observed an event rate ratio on 1.07 (95% CI: 1.06, 1.07) in strict regulatory regimes and 1.09 (95% CI: 1.09, 1.10) in weak regulatory regimes. Peer influence did not vary by regulatory environment for Invega and Pristiq.

While the previous set of models demonstrated that there was an elevated and statistically significant association between peer prescribing and the focal physician’s prescribing rate of Vyvanse and Cymbalta in areas with marketing regulation in the first year the medication was on the market, the peer effects we observed for Vyvanse and Cymbalta likely vary over time. Just as we have seen that peer effects vary by regulatory environment, they also likely vary across time. To test this assertion, we limited our analysis to the first four months the medication was on the market. The results of
these models are presented in Table 5. For both Cymbalta and Vyvanse, peer influence has the largest impact on physician prescribing behavior in the months just after the new medication is introduced—particularly in areas with strict regulation governing interactions between physicians and the pharmaceutical industry. In the first four months after introduction, the event rate ratio for the interaction between strict policy and peer influence was 1.13 (95% CI: 1.10, 1.16) for Vyvanse and 1.19 (95% CI: 1.06, 1.32) for Cymbalta. The event rate ratio for peer influence in strict regulatory regimes was 1.70 (95% CI: 1.44, 1.99) in the first month Vyvanse was introduced but diminished over time.9 Over time, the importance of peer effects diminishes as knowledge about the new drug has diffused. Recall, that we do not have data for the first months after Cymbalta is introduced and only begin observing prescribing behavior five months after introduction. There are still strong regulatory effects in strict regimes in the first quarter of observation. This effect size is similar to what we observe for Vyvanse during the same period. Thus, it appears that peer influence may be most important role for diffusing knowledge about drugs just after they are introduced, particularly in markets with pharmaceutical marketing regulation.

Table 5 About Here

To better understand how regulation and peer influence shape markets for newly introduced psychotropic medications, we generated predicted prescribing rates for Vyvanse, Cymbalta, Pristiq and Invega based on the models reported in Table 4. As Figures 2 shows, baseline prescribing rates for all four newly introduced medications (shown in grey) were lower in states with marketing regulation than in states that did not restrict pharmaceutical detailing. However, in strict regulatory regimes peer networks offered an alternative pathway through which physicians could learn about

9The full set of models stratified by month are available upon request.
drugs that had some comparative advantages over other medications already on the market. In areas with stringent marketing regulation, peer influence (shown in black) acted as a substitute for marketing effects. Prescribing rates of innovative medications, here Cymbalta and Vyvanse, in areas with unrestricted marketing did not statistically differ from prescribing rates in strict regulatory regimes once peer influence was taken into account. In areas with weaker marketing regulation, we still see lower baseline prescribing rates but peer effects are only have a significant effect on Vyvanse prescribing. Peer influence had no meaningful impact on the probability that a physician would prescribe Pristiq or Invega. In sum, for drugs that afford advantages over existing alternatives, peer effects act as a substitute for detailing when state law substantially limits marketing efforts. For less efficacious medications that offer no improvement, marketing regulations simply reduce prescribing.

Robustness Checks

We conducted several robustness checks to ensure that the peer effects we observe did not arise from serial dependence in physician behavior, joint environmental effects on the physician and his or her peers, and to ensure that the peer effects we observe did not arise from homophily. Each of these analyses increased our confidence in our results. Models incorporating physician fixed effects increased our confidence in our results and assuaged concerns that targeting bias or omitted physician characteristics might explain our results. With physician fixed effects the peer influence coefficient for Cymbalta was 1.08 (95% CI: 1.04, 1.12) and 1.12 (95% CI: 1.11, 1.14) for Vyvanse in strict regulatory regimes. Similarly, estimates of peer influence remained robust to the inclusion of physician fixed effects in states with weaker marketing restrictions.
Incorporating estimates of marketing expenditures and zip code fixed effects did not substantially alter our results. The inclusion of estimates of marketing expenditures had no effect on the main peer influence variable for either Vyvanse or Cymbalta. For Vyvanse, including marketing expenditures resulted in a significant reduction in the coefficient for the interaction between weak regulation and peer influence. Incorporating marketing expenditures reduced the coefficient from 1.07 (95% CI: 1.06, 1.07) to 1.02 (95% CI: 1.02, 1.02). For Cymbalta, models with and without marketing expenditures produced coefficients identical to two decimal for the variables of interest. Similarly, as shown in Table 7, the results of our analyses were robust to the inclusion of three-digit zip code fixed effects.

Moreover, two additional factors increased our confidence in our results. First, we only observe peer effects in areas with limited marketing influence. If marketing or homophily were driving our results, we would expect to observe peer effects in all areas. In addition, we only see significant peer effects for efficacious drugs. If homophily accounted for the peer effects in our model, we would not expect it to express only on efficacious medications. Any alternative explanation of our results must simultaneously account for the expression of peer effects only in circumstances in which marketing regulation is in place and the drug is efficacious.

**Limitations**

Our study is limited in its ability to establish causality and the mechanisms by which regulation and peer effects operate. Since we do not have data on prescribing behavior pre- and post- policy
implementation, it is difficult to establish whether the policy itself accounts for the observed association between regulatory environment and lower prescribing rates or whether there is something different about these areas that leads them to adopt policies regulating pharmaceutical marketing activity and to have lower prescribing rates irrespective of the policy. To help disentangle these two possible competing explanations, we conducted two additional analyses. First, we conducted a supplementary analysis that included a dummy variable to examine prescribing behavior in Colorado. In 2006, legislation that would have required and made public disclosures of payments to the physician passed both the house and the senate but was vetoed by the Governor. If political climate or practice preferences accounted for the observed variation by regulatory environment, we would anticipate lower rates of prescribing in Colorado relative to states that have not passed marketing legislation. The robustness check found no evidence that this was the case: the event rate ratio for Colorado was 0.87 (95% C.I: 0.65, 1.15) for Vyvanse, Pristiq was 0.76 (95% C.I: 0.55, 1.04), Invega was 1.30 (95% C.I: 1.11, 1.52) and Cymbalta was 0.91 (0.80, 1.04). Finally, we were able to obtain additional data for the antipsychotic class for the period in which Vermont strengthened its marketing regulation, which allowed us to observe prescribing rates of Invega prior to policy implementation and after the stronger policy took effect. A comparison of prescribing behavior pre- and post- policy implementation is striking. Following the enactment of more stringent policy, prescribing rates of Invega drop by half and never reach their previous levels. While it does appear that prescribing rates eventually start to increase once again, they never reach their prior levels. Although future research is needed, the available evidence suggest that policies regulating marketing and detailing may have a causal effect on prescribing behavior. This is consistent with prior research.

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10 The additional data was obtained for reason unrelated to this study. Unfortunately, due to the expense of obtaining the data this was the only class we were able to obtain through the current period. Since the antipsychotic class is considerably smaller in terms of number of prescriptions written, it is the most affordable class to obtain and it is also the most dynamic. The drawback is that prescribing rates of these medications are relatively rare, so test of statistical significance using the Vermont data alone are not feasible.
using a difference in differences approach which found that the adoption of conflict of interest policies by medical schools led to lower rates of prescribing of newly marketed mental health medications (King, Essick, Ross, and Bearman 2013). A second question our study cannot adequately address that warrants further investigation is how these policies work to reduce prescribing. For instance, do pharmaceutical companies reduce marketing efforts when faced with regulation or are physicians less likely to respond favorably to detailing when faced with disclosure? Future research examining how these policies work could be informative for efforts to reduce costs and encourage innovation within the pharmaceutical sector, but could also provide valuable insight for other efforts to reform and transform markets through information based regulation.

Discussion and Conclusion

Over fifty years ago, Coleman, Katz, and Menzel transformed sociological understandings of innovation by highlighting the importance of social influence in the spread of a new medication. Since “The Diffusion of an Innovation among Physicians” was published, it has been “a strategic research site for testing new propositions of how social structure drives contagion” (Burt 1987: 103). Within this context, one of the most salient changes in the past five decades has been the exponential increase in marketing expenditures by pharmaceutical companies, especially expenditures directed towards detailing. In response to the dramatic rise in pharmaceutical detailing and gift giving, states have implemented policies to reduce potential conflicts of interest generated by pharmaceutical marketing and promote evidence based medicine.

We find that regulation of pharmaceutical marketing had a significant impact on physicians’ propensity to prescribe four newly introduced medications, which are considerably more expensive than comparable existing alternatives. The large declines in prescribing we observe in areas with both stringent and weaker forms of marketing regulation are surprising in light of work in social
psychology predicting that information based regulation and soft gift bans would be ineffective (Dana and Lowenstein 2003).

Critically, marketing regulation did not simply reduce prescribing for all medications. For medications that did afford advantages over other drugs already on the market, peer effects offer an alternative means by which information about new drugs can diffuse when regulations are in place restricting pharmaceutical marketing. When regulation does not exist to limit or restrict marketing efforts, peers do not seem to be an important source of information about new medications. Instead, marketing efforts are likely the primary means by which physicians learn about new medications. These findings have important implications for understandings of innovation, regulation, and market transformation, as well as for public policy.

With respect to the literature on diffusion, innovation, and regulation, our work augments and extends a long history of sociological inquiry into the role of marketing and peer effects in the diffusion of medical innovations. Much of the literature on diffusion focuses on the diffusion of products, processes, and policies that eventually become widely adopted and are successful. Our work helps correct this bias by examining patterns of diffusion of medications that vary in innovativeness. In addition, our work demonstrates that both the extent to which products diffuse, as well as the pathways by which products diffuse vary depending on the characteristics of the innovation and environmental context.

In showing that the regulation shaped both the extent to which and pathway by which diffusion occurred, we add to a growing body of experimental and empirical research analyzing sof-regulation and market transformation. The indirect effects of pharmaceutical marketing regulation we observe are arguably as important as the direct effects. When an innovative drug comes to market, if detailing is prohibited, it is imperative that physicians have alternatives ways to learn about it. We
find that peer effects substitute for detailing and allow for the diffusion of information about new drugs through channels less subject to conflicts of interest.

It is often argued that regulation stymies innovation. In this article, we have shown that within the pharmaceutical sector, rather than hindering innovation, regulation may actually encourage innovation by intensifying market pressures to produce medications that are improvements over existing alternatives. In the face of strict marketing regulation, drugs that are simply reformulations do not sell. Good drugs don’t sell themselves, but in medicine, peers influence others to prescribe drugs that work and do not influence each other to prescribe drugs that don’t work. Detailing, in contrast, influences physicians to prescribe drugs that offer limited, if any, value. That is why, of course, the pharmaceutical industry spends billions of dollars a year on detailing. Regulatory regimes that curtail such largess turn out to benefit consumers, since in the absence of gifts, dinners, honoraria, pens, trips, free samples, and other inducements, physicians turn to other physicians for advice about new drugs, select drugs that work and ignore those that do not. Thus, the direct and indirect consequences of regulation collectively can lead to market transformation and may stimulate deeper and ultimately more beneficial innovation.
Figure 1. Average number of prescriptions written per month by physicians with peers. Due to data availability Cymbalta prescribing starts in month five.
Figure 2a. Predicted number of Cymbalta and Vyvanse prescriptions written in an average month by an average physician practicing in different marketing regulatory environments. Predicted prescribing rates are shown without peer effects (grey) and with peer effects at one standard deviation above the mean (black).
Figure 2b. Predicted probability of an average physician prescribing Invega and Pristiq in an average month by marketing regulatory environments. Predicted prescribing rates are shown without peer effects (grey) and with peer effects at one standard deviation above the mean (black).
### Table 1. Characteristics of policies regulating pharmaceutical marketing activity by state in 2009.
Policy in Massachusetts was enacted after our study period.

<table>
<thead>
<tr>
<th>Code of Conduct</th>
<th>CA</th>
<th>NV</th>
<th>DC</th>
<th>ME</th>
<th>WV</th>
<th>MA</th>
<th>VT</th>
<th>MN</th>
</tr>
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<tbody>
<tr>
<td>Any Disclosure Requirement</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Gift Limits Based on PhRMA Code</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td>Statutory Gift Ban</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
</tbody>
</table>

### Table 2. Characteristics of medications introduced during the study period. The number of prescriptions is the number of prescriptions written for the medication in the first 12 months after its introduction. Since we only observe Cymbalta from month four on, the total number of prescriptions is the number of scripts written between month four and twelve.

<table>
<thead>
<tr>
<th>Name</th>
<th>Class</th>
<th>Introduced</th>
<th>Prescriptions</th>
<th>Therapeutic Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cymbalta</td>
<td>Antidepressant</td>
<td>8/2004</td>
<td>1,313,938</td>
<td>Indication for pain and Fibromyalgia.</td>
</tr>
<tr>
<td>Invega</td>
<td>Antipsychotic</td>
<td>12/2006</td>
<td>170,623</td>
<td>Reformulation. Little or no improvement.</td>
</tr>
<tr>
<td>Pristiq</td>
<td>Antidepressant</td>
<td>2/2008</td>
<td>573,298</td>
<td>Reformulation. Little or no improvement.</td>
</tr>
<tr>
<td>CYMBALTA</td>
<td>VYVANSE</td>
<td>INVEGA</td>
<td>PRISTIQ</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>---------</td>
<td>--------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>IRR</td>
<td>95% CI</td>
<td>IRR</td>
<td>95% CI</td>
<td>OR</td>
</tr>
<tr>
<td>Strong Policy</td>
<td>0.73*** (0.70, 0.77)</td>
<td>0.57*** (0.54, 0.61)</td>
<td>0.66** (0.50, 0.87)</td>
<td>0.27*** (0.20, 0.35)</td>
</tr>
<tr>
<td>Weak Policy</td>
<td>0.60*** (0.58, 0.61)</td>
<td>0.55*** (0.54, 0.57)</td>
<td>0.65*** (0.58, 0.73)</td>
<td>0.67*** (0.59, 0.76)</td>
</tr>
<tr>
<td>Lagged DV</td>
<td>1.04*** (1.04, 1.04)</td>
<td>1.01*** (1.01, 1.01)</td>
<td>10.01*** (9.10, 11.00)</td>
<td>25.6*** (25.2, 26.0)</td>
</tr>
<tr>
<td>Graduation Year</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.01 (1.01, 1.01)</td>
</tr>
<tr>
<td>% Medicaid</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.27*** (1.19, 1.35)</td>
<td>0.99*** (0.99, 0.99)</td>
</tr>
<tr>
<td>% Cash</td>
<td>1.00*** (1.00, 1.00)</td>
<td>0.99*** (0.99, 0.99)</td>
<td>0.81 (0.53, 1.26)</td>
<td>0.99** (0.99, 0.99)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>9.43*** (8.30, 10.71)</td>
<td>1.39*** (1.37, 1.41)</td>
<td>1.01*** (1.01, 1.01)</td>
<td></td>
</tr>
<tr>
<td>Generalist</td>
<td>0.79*** (0.79, 0.79)</td>
<td>0.60*** (0.60, 0.62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume Exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Regulatory strength and prescribing rates of newly introduced mental health medications in the first year medication was on the market. Omitted categories include third-party payment and no pharmaceutical regulation*** indicates significant at p<0.001.
Table 4. Regulatory strength, peer influence, and prescribing rates of newly introduced mental health medications. Omitted categories include third-party payment and no pharmaceutical regulation. All models include data from the first year the medication is on the market, except for Cymbalta which only includes data from the fifth month through twelfth month the medication was on the market due to data availability. *** p<0.001, ** p<0.01, * p<0.05

<table>
<thead>
<tr>
<th></th>
<th>CYMBALTA</th>
<th>VYVANSE</th>
<th>INVEGA</th>
<th>PRISTIQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong*Peer Influence</td>
<td>1.11*** (1.08, 1.14)</td>
<td>1.07*** (1.06, 1.07)</td>
<td>1.18 (0.80, 1.74)</td>
<td>0.70 (0.39, 1.28)</td>
</tr>
<tr>
<td>Weak*Peer Influence</td>
<td>1.03*** (1.01, 1.04)</td>
<td>1.09*** (1.09, 1.10)</td>
<td>0.98 (0.78, 1.23)</td>
<td>1.04 (0.91, 1.11)</td>
</tr>
<tr>
<td>Strong Policy</td>
<td>0.56*** (0.50, 0.62)</td>
<td>0.61*** (0.53, 0.71)</td>
<td>0.59*** (0.46, 0.76)</td>
<td>0.22*** (0.25, 0.33)</td>
</tr>
<tr>
<td>Weak Policy</td>
<td>0.52*** (0.49, 0.55)</td>
<td>0.58*** (0.51, 0.66)</td>
<td>0.71** (0.56, 0.91)</td>
<td>0.52*** (0.43, 0.63)</td>
</tr>
<tr>
<td>Peer Influence</td>
<td>1.01** (1.00, 1.01)</td>
<td>1.02*** (1.02, 1.02)</td>
<td>1.04 (0.99, 1.08)</td>
<td>1.02*** (1.01, 1.04)</td>
</tr>
<tr>
<td>Prescribing t-1</td>
<td>1.09*** (1.09, 1.09)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>8.26*** (6.40, 10.67)</td>
<td>15.7*** (15.2, 16.3)</td>
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<tr>
<td>Lagged Peer Volume</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
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<tr>
<td>Graduation Year</td>
<td>1.00** (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00 (0.99, 1.01)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>% Medicaid</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.00*** (1.00, 1.00)</td>
<td>1.01*** (1.00, 1.01)</td>
<td>0.98*** (0.98, 0.99)</td>
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<tr>
<td>% Cash</td>
<td>1.00*** (1.00, 1.00)</td>
<td>0.99*** (0.99, 0.99)</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.00*** (0.99, 1.00)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td></td>
<td>8.26*** (6.40, 10.67)</td>
<td>1.27*** (1.19, 1.34)</td>
<td></td>
</tr>
<tr>
<td>Generalist</td>
<td>1.01 (0.99, 1.02)</td>
<td>0.62*** (0.60, 0.64)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume Exposure</td>
<td>1.02*** (1.02, 1.03)</td>
<td>1.01*** (1.01, 1.01)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician Months</td>
<td>208,072</td>
<td>215,445</td>
<td>115,388</td>
<td>385,447</td>
</tr>
<tr>
<td></td>
<td>CYMBALTA</td>
<td>VYVANSE</td>
<td>INVEGA</td>
<td>PRISTIQ</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Strong*Peer Influence</td>
<td>1.19***</td>
<td>(1.06, 1.32)</td>
<td>1.13***</td>
<td>(1.10, 1.16)</td>
</tr>
<tr>
<td>Weak*Peer Influence</td>
<td>1.04***</td>
<td>(1.01, 1.07)</td>
<td>1.02***</td>
<td>(1.01, 1.03)</td>
</tr>
<tr>
<td>Strong Policy</td>
<td>0.50***</td>
<td>(0.38, 0.65)</td>
<td>0.55***</td>
<td>(0.38, 0.79)</td>
</tr>
<tr>
<td>Weak Policy</td>
<td>0.55***</td>
<td>(0.47, 0.63)</td>
<td>1.07</td>
<td>(0.93, 1.22)</td>
</tr>
<tr>
<td>Peer Influence</td>
<td>1.01*</td>
<td>(1.00, 1.02)</td>
<td>1.04***</td>
<td>(1.03, 1.04)</td>
</tr>
<tr>
<td>Any Policy</td>
<td></td>
<td></td>
<td>0.67*</td>
<td>(0.46, 0.97)</td>
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<tr>
<td>Any*Peer Influence</td>
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<td></td>
<td>1.07</td>
<td>(0.63, 1.81)</td>
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<tr>
<td>Prescribing t-1</td>
<td>1.12***</td>
<td>(1.11, 1.13)</td>
<td>1.00</td>
<td>(0.99, 1.00)</td>
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<tr>
<td>Lagged Peer Volume</td>
<td>1.00*</td>
<td>(1.00, 1.00)</td>
<td>1.00***</td>
<td>(1.00, 1.00)</td>
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<tr>
<td>Graduation Year</td>
<td>1.00</td>
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<td>1.00***</td>
<td>(1.00, 1.00)</td>
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<tr>
<td>% Medicaid</td>
<td>1.01***</td>
<td>(1.00, 1.01)</td>
<td>0.99***</td>
<td>(0.99, 0.99)</td>
</tr>
<tr>
<td>% Cash</td>
<td>1.00**</td>
<td>(1.00, 1.01)</td>
<td>0.99***</td>
<td>(0.99, 0.99)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td></td>
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<tr>
<td>Generalist</td>
<td>1.07***</td>
<td>(1.01, 1.13)</td>
<td>0.64***</td>
<td>(0.59, 0.69)</td>
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<tr>
<td>Volume</td>
<td>Exposure</td>
<td>Exposure</td>
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Table 5. *** p<0.001, ** p<0.01, * p<0.05. Omitted categories include third-party payment and no pharmaceutical regulation. Models include first four months the medication is on the market, except for Cymbalta which only include the fourth month on market due to data availability.
<table>
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<th>Vyvanse</th>
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<tr>
<td></td>
<td>IRR</td>
<td>95% CI</td>
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<td>95% CI</td>
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<td>Strict Policy</td>
<td>1.08***</td>
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<td>1.12***</td>
<td>(1.11, 1.14)</td>
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<td>1.03***</td>
<td>(1.01, 1.05)</td>
<td>1.05***</td>
<td>(1.05, 1.06)</td>
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<td>Physician Fixed Effects</td>
<td>Yes</td>
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<td>Yes</td>
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<td>Strict Physician Months</td>
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<td>Weak Physician Months</td>
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<td>8,383</td>
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<tr>
<td>No Policy Physician Months</td>
<td>87,270</td>
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<td>63,977</td>
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Table 6.*** p<0.001, ** p<0.01, * p<0.05 . Estimates of peer influence with physician fixed effects. Models include controls for payment composition, graduation year, lagged peer prescribing volume, as well as a volume as an exposure variable. Vyvanse models include data from the first year the medication is on the market. Cymbalta models only include data from the fifth month through twelfth month the medication was on the market due to data availability.
Table 7. Peer influence in strict and weak regulatory regimes with three-digit zip code fixed effects. Omitted categories include third-party payment and no pharmaceutical regulation. All models include first year the medication is on the market, except for Cymbalta which only includes the fourth through eighth month on market due to data availability. *** p<0.001, ** p<0.01, * p<0.05.
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Wejnert, B.

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<th>CYMBALTA</th>
<th>VYVANSE</th>
<th>INVEGA</th>
<th>PRISTIQ</th>
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<tr>
<td>Avg. # Scripts/Month</td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
<td>Mean 95% CI</td>
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<tr>
<td>No Regulation</td>
<td>0.69 (0.68, 0.70)</td>
<td>0.48 (0.46, 0.49)</td>
<td>0.07 (0.07, 0.07)</td>
<td>0.08 (0.08, 0.08)</td>
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<td>Weak Regulation</td>
<td>0.41 (0.38, 0.43)</td>
<td>0.10 (0.09, 0.11)</td>
<td>0.04 (0.04, 0.05)</td>
<td>0.03 (0.03, 0.03)</td>
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<tr>
<td>Strict Regulation</td>
<td>0.23 (0.21, .025)</td>
<td>0.15 (0.13, 0.17)</td>
<td>0.02 (0.01, 0.20)</td>
<td>0.01 (0.01, 0.01)</td>
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<tr>
<td>Independent Variables</td>
<td>Mean  SD</td>
<td>Mean  S.D</td>
<td>Mean  S.D</td>
<td>Mean  S.D</td>
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<td>Strong Policy</td>
<td>0.05 0.22</td>
<td>0.05 0.21</td>
<td>0.05 0.22</td>
<td>0.5 0.21</td>
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<tr>
<td>Weak Policy</td>
<td>0.11 0.31</td>
<td>0.15 0.35</td>
<td>0.09 0.29</td>
<td>0.10 0.31</td>
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<tr>
<td>Lagged DV</td>
<td>0.59 1.92</td>
<td>0.36 2.59</td>
<td>0.07 0.80</td>
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<tr>
<td>% Third Party</td>
<td>80.28 25.48</td>
<td>82.02 27.61</td>
<td>80.75 3045</td>
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<td>% Medicaid</td>
<td>11.35 21.82</td>
<td>9.45 22.05</td>
<td>13.88 27.16</td>
<td>5.68 15.5</td>
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<tr>
<td>% Cash</td>
<td>8.37 15.44</td>
<td>8.55 19.16</td>
<td>5.37 16.43</td>
<td>7.84 15.45</td>
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<tr>
<td>Psychiatrist</td>
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<td>0.20 0.40</td>
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<td>Generalist</td>
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<td>0.44 0.50</td>
<td>0.44 0.50</td>
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<tr>
<td>Volume</td>
<td>28.2 36.1</td>
<td>10.90 20.34</td>
<td>7.78 18.82</td>
<td>33.44 44.45</td>
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<td>Lagged Peer Focal Drug</td>
<td>1.13 3.20</td>
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<td>0.06 0.66</td>
<td>0.22 1.19</td>
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<tr>
<td>Lagged Peer Vol.</td>
<td>42.4 56.67</td>
<td>25.67 38.29</td>
<td>14.58 34.40</td>
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<td>N Prescriptions in Class</td>
<td>5,501,804</td>
<td>2,904,241</td>
<td>1,374,477</td>
<td>14,121,161</td>
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Appendix A. Descriptive statistics for prescriptions written by physicians with peers.