

# How Inefficient are Markets for Technology?

Manuel Hermosilla<sup>1</sup> and Yufei Wu<sup>2</sup>

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PRELIMINARY AND INCOMPLETE

## Abstract

Previous literature shows that contracting frictions may preclude valuable cooperation between innovators and commercializers in Markets for Technology. This literature, however, does not address the question of how large the implied inefficiency is. Focusing on licensing-based cooperation in the pharmaceutical industry and the enactment of the Medicare Part D program (which implied a large downstream demand shock for selected technologies), we provide evidence suggesting that efficiency is not severely undermined in this market. Our results suggest that while contracting frictions preclude some cooperation; they do not do so for the 75% of technologies for which potential gains of cooperation are the largest. The implied efficiency burden is therefore much lower than what could be estimated based on the number of “failed cooperation deals” alone. Our results further document a vigorous, short-termed cooperation response to the program’s enactment, suggesting that commercializers may effectively perform the intermediary role of sourcing from the Market for Technology to satisfy consumer demand.

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<sup>1</sup> The Johns Hopkins Carey Business School. Email: [mh@jhu.edu](mailto:mh@jhu.edu). Corresponding author.

<sup>2</sup> MIT, Economics Department. Email: [yufeiwu@mit.edu](mailto:yufeiwu@mit.edu).

# 1. Introduction

The trade of knowledge-based intermediate inputs in Markets for Technology (MFT) has become an important pillar for inter-firm cooperation aimed for the innovation of new products. Fueled by deepening technological and marketing complexity, these markets create gains by promoting specialization (Arora et al., 2001), avoiding replicative investments in the so-called “complementary assets” (Teece, 1986; Gans et al., 2002; Gans and Stern, 2003; Galasso et al., 2010), and preserving market power (Gans et al., 2002; Gans and Stern, 2003). Vibrant MFTs can be traced back to the late nineteenth century in select industries (Lamoreaux and Sokoloff, 1999) but since then new arenas of trade have emerged and aggregately grown (outpacing GDP) to a total of over \$100 billion in annual transactions (Arora and Gambardella, 2010).

Exchange in these markets faces challenges grounded on the very nature of the traded assets. The imperfect appropriability of knowledge may dissuade agents from engaging in trade for the fear of having their ideas expropriated (Arrow, 1962; Anton and Yao, 1994). Even when intellectual property protection is possible, uncertainty regarding its extent and scope may preclude or delay cooperation (Gans et al., 2002; Gans et al., 2008). Costly and lengthy processes of search for partners (Hellman, 2007; Agrawal et al., 2014) and arduous contract negotiations imply monetary and alternative costs (Lerner and Merces, 1998; Agrawal et al., 2014). These are further compounded by the significant uncertainty and informational asymmetries stemming from the novelty and complexity of new technologies, which make it hard to evaluate their technical and commercial merits, and ultimately agree to “fair” terms of cooperation (Agrawal et al., 2014). These frictions are commonly referred to as transaction costs as they may impede the materialization of valuable cooperation agreements.

Owing to these considerations, a presumption of inefficiency looms over MFT. In an efficient market, cooperation would pair innovators with commercializers to maximize benefits of complementary expertise and avoid replicative investment. Furthermore, to the extent that the benefits of complementary expertise can be exploited during a product’s development, cooperation would be initiated early on in the process. Previous research has produced evidence that characterizes the impacts of the individual types of

transaction costs, convincingly arguing that these operate in the market and preclude *some cooperation*. Yet, to the best of our knowledge, there has been no deliberate attempt to provide context by sizing their aggregate efficiency burden. We see this as an important gap, as the nature of policy implications and emphasis of future research ought to depend on whether we find ourselves in a situation in which little or great value is lost to cooperation that fails to materialize. Focusing on licensing-based cooperation on the drug development industry (where biotech firms play the role of upstream innovators and large “Big Pharma” corporations that of downstream commercializers), this paper constitutes a first step to elucidate this.

An assessment of the efficiency burden imposed by transaction costs on MFTs that solely relies on the number of cooperation agreements would be correct if the value of cooperation was homogeneous across technologies. However, even within an industry, technologies may vary widely in this respect. Variation can stem from the characteristics of the downstream (narrowly defined) market (Gans et al., 2002; Gans and Stern, 2003) or from the degree of dependence on complementary assets created by the technology’s design (Teece, 1986).

The latter effect is notoriously heterogeneous across technologies in the industry under study. The dissemination of information required to generate adoption of new drug therapies heavily relies on promotional visits by pharmaceutical representatives to prescribing physicians. Failure to strike a cooperation agreement forces an innovator without market presence to assemble, train and maintain its own contingent of representatives. When cooperation is in place, however, these costs are spread out over the many drugs in the downstream commercializers’ wide portfolios. This means that cooperation leads to higher average profit margins through the exploitation of scope economies in distribution. In this context, therapies prescribed by large populations of physicians benefit from cooperation more than those with smaller populations. To illustrate the heterogeneity stemming from the dependence on this type of complementary asset figure 1 shows the distribution of the number of prescribing physicians (NPP) among compounds in our main data set.<sup>1</sup>

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<sup>1</sup> We explain the construction of this variable in section 4.

We provide two sets of results suggesting that the majority of high-value cooperation is not precluded by transaction costs. First we examine the patterns of licensing-based cooperation within a large sample of developing compounds. We find that rates of cooperation are overall high, and strongly increasing in the NPP measure. This last result serves a validation for NPP as a leading determinant of the technology-specific value of cooperation and supports the notion that transaction costs do not severely undermine the realization of gains from cooperation when it matters the most. Nevertheless, it is still vulnerable to the possibility that other sources of value may remain vastly unexploited, for example, because deals are struck in untimely fashion or because inefficient matching destroys market power.

Our second set of analysis attempts to moderate this problem by studying the anatomy of the *cooperation response* to the downstream demand shock implied by the 2003 enactment of Medicare Part D (“Part D”). This program constituted a large expansion of the reimbursement coverage for prescription drug expenditures of Medicare enrollees (65yo+), effectively expanding downstream demand for selected therapies (those that are more prevalent among Medicare enrollees.) Focusing on the number of licensing deals aimed for the commercialization of compounds in territories that include the U.S., figure 2 evidences a strong increase in the extent of cooperation among compounds with high exposure to the shock (solid line) relative to that among compounds with low exposure (dashed line).<sup>2</sup> Figure 3 replicates these trends among licensing deals that did not include U.S. commercialization. In this case, there is no exposure-mediated difference, reassuring us of the effect’s exogeneity.

As we show with a simple model, transaction costs of different magnitudes imply markedly different patterns of the cooperation response along the distribution of cooperation values. If transaction costs are relatively high, the cooperation response will mostly draw from technologies in upper ranges of the distribution. In contrast, if transaction costs are relatively low, the cooperation response will mostly draw from the bottom of this distribution. The intuition is simple: the higher transaction costs are, the

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<sup>2</sup> To determine a compound’s degree of exposure to the demand shock we follow the approach of Duggan and Scott-Morton (2011), Blume-Kohout and Sood (2013) and Dranove et al. (2014) by computing the “Medicare Market Share” variable. In section 5 we explain the details of the procedure.

higher the cooperation value associated to the inframarginal technology is. Our results support the brighter scenario in which transaction costs are moderate, suggesting that they effectively preclude cooperation only for those technologies at the bottom quartile of the distribution of cooperation.

Further analysis suggests that the cooperation response was instantaneous and focused on the licensing of compounds that were undergoing clinical trials. Given the long drug development cycles, this suggests that the increased volume of licensing-based cooperation was not an artifact of an “endogenous supply” effect. It also suggests that the effect may have operated in the form of facilitating negotiations that were ongoing at the time the program was enacted, as a higher downstream demand increases the size of the bargaining core and makes it easier for firms to agree to “fair” terms (Lerner et al., 2002).

The current MFT literature displays a marked focus on the supply side or, as Arora and Gambardella (2010) put it, “the factors that lead companies to license or sell technology, the implications thereof [...] and the conditions that facilitate the rise of technology specialists.”<sup>3</sup> Our research contributes to this literature by offering a more panoramic view, one in which firms on the demand side of MFT act as *agents for commercialization* whose main role is to source embryonic technologies from the MFT, employ their capabilities to develop them into final products and allocate them to consumer demand. While we do not directly analyze these firms’ behavior, we interpret the vigorous cooperation response to Part D as an auspicious sign, as it suggests that these “technology demandants” effectively perform this role by agilely reacting to satisfy market opportunities.<sup>4</sup> Carefully interpreted, the strong cooperation response is also a good sign in that it suggests that MFT could be effectively performing a screening role: failed cooperation could in part signal the “weeding out” of technologies “pushed” by innovators for which market potential is not large enough to justify the commercialization effort.

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<sup>3</sup> Two exceptions are Cassiman and Veugelers (2006) and Forman et al. (2008), who focus on the question of how firms’ characteristics (or the environment they operate on) affect their demand for external technology

<sup>4</sup> Furthermore, because we only focus on cooperation in the form of commercialization licensing deals, these estimates may underestimate the true extent of cooperation in the market place, as share of it takes place in the form of Mergers and Acquisitions (Gans et al., 2002; Higgins and Rodriguez, 2006).

In the remainder of the paper we present a theoretical framework and empirical strategy (section 2) and describe the licensing data (section 3). We then describe the construction and validation of our proxy for the value of cooperation (section 4). We continue by providing an overview of Part D and the measurement of the implied demand shock across therapeutic categories (section 5) and documenting the cooperation response (Section 6). In section 7 we delve into the possibility of potentially confounding endogenous supply effects and conclude in section 8 discussing and summarizing our main results.

## 2. Analytical Framework

The purpose of the framework developed here is not to provide an accurate description of the types of interactions or behavior (e.g., search, matching) that may be conducive to cooperation agreements in MFT, but to lay out a model to guide the interpretation of the empirical results and set up the identification strategy. The model is therefore silent about the way rents accrued from cooperation are divided between contracting parties, or how private benefits may prompt agents' collaboration, or what the specifics of the matching process are. Instead it provides a simple characterization of the economic fundamentals that can support cooperation because they generate a higher total profit than its alternative (i.e., no cooperation or "self-commercialization"), assuming agents will find a way to divide profits (possibly at a cost). The section is divided in two parts, a first in which we present the basic analytic framework, and a second in which we describe the empirical strategy.

### 2.1 Theory

We consider a static setting in which each upstream innovator ( $i = 1, \dots, I$ ) has a new technology. Each innovator has a single technology, so both technologies and innovators are indexed by  $i$ . The new technology could either be seen as a product that is ready to be commercialized or the core technological component over which a new

technology product can be developed.<sup>5</sup> Its potential for use is narrow in scope, that is, it is not a general-purpose technology and targets a well-defined market. The technology could reach the market either through cooperation with a downstream commercializer ( $j = 1, \dots, J$ ) or self-commercialization by the innovator (i.e., no cooperation).

Downstream commercializers are endowed with a commercialization advantage. This occurs because they are able to deliver higher average profit margins, either because they possess complementary assets<sup>6</sup> or because they have market power in the downstream market. Below we describe how these can be justified in the context of the pharmaceutical industry.

A technology's total expected profits (or consumer demand, or market potential) under self-commercialization is denoted by  $D_i$ .<sup>7</sup> One can think of  $D_i$  as the total willingness to pay that the innovator will be able to capture on its own, net of any investments done for that purpose.

Under cooperation, a technology's total expected profits are larger as the capabilities of a downstream commercializer are employed. We denote total expected profits in this case as  $D_i m_{ij}$ , where  $m_{ij} \geq 1$  is the *cooperation multiplier*, which reflects the additional value stemming from the synergies of cooperative commercialization when a match with a commercializer  $j$  is in place.

In the pharmaceutical industry, the cooperation multiplier can be justified by the extensive market knowledge, brand recognition and downstream market power of established Big Pharma commercializers.<sup>8</sup> Another important determinant stems from

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<sup>5</sup> In this case we assume that development is immediate and riskless, and associated costs are zero.

<sup>6</sup> For example, commercializers with brand recognition may be able to charge a higher price to consumers. Alternatively, commercializers with established distribution channels can spread associated fixed costs among all commercialized technologies in their portfolios, leading to lower average distribution costs.

<sup>7</sup> Aside from behind-the-scenes and cross-industry variation, the role of downstream consumer demand remains unexplored in the related empirical literature. An exception arises in the literature examining the impact of intellectual property protection on international technology transfer (e.g., Branstetter et al., 2006; Delgado et al., 2013), where increases in market potential are identified after countries boost enforcement of intellectual property rights laws.

<sup>8</sup> High concentration within therapeutic areas (Malerba and Orsenigo, 2002) warrants the existence of losses due to enhanced competition. Another source of cooperation value lies on downstream commercializers' potential regulatory advantage, acquired throughout their long histories of interactions with the FDA. This advantage can translate in a higher probability of obtaining regulatory approval, but also in faster time-to-market (Dranove and Meltzer, 1994).

their established distribution channels. Promotional activities heavily rely on visits to physicians by sales representatives (Silverman, 2014) and have traditionally claimed a significant share of industry revenues (Donohue et al., 2007).<sup>9</sup> For a biotech innovator without presence in the downstream market, self-commercialization therefore implies investing in assembling and training a sales force, a fixed cost that translates into lower average margins. This means that cooperation can be valuable if replicative investment is avoided.

Based on the idea that some technologies can benefit from cooperation more than others, we define the cooperation multiplier as being driven by a main technology-specific effect ( $V_i$ ) and a match-specific deviation ( $M_{ij}$ ). We specify it as

$$m_{ij} = 1 + V_i M_{ij}$$

with  $V_i, M_{ij} \in [0,1]$ , and independently distributed according to  $F^V$  and  $F^M$ , respectively. Thus,  $V_i$  reflects the average the extent of cooperation gains when the best possible match is materialized ( $M_{ij} = 1$ ). Poorer matches ( $M_{ij} < 1$ ) erode these gains and, in the extreme, can completely eliminate them ( $M_{ij} = 0$ ).

The final component of the model is a transaction cost, which we denote by  $C$  and assume is paid every time cooperation happens. Given the nature of our empirical exercise, we define it broadly, including the alternative cost of time and the monetary costs implied by the search of partners and negotiation of a cooperation agreement (i.e., the allocation of control rights and division of profits),<sup>10</sup> which entails comprehensive due diligence and bargaining to reach agreement over a wide range of control and residual rights (Lerner and Merges, 1998; Lerner et al., 2004; Lerner and Malmendier, 2006). Crucially, the success of negotiations is contingent on firms agreeing to “fair” terms, an elusive requirement given the novelty and complexity of implied technologies

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<sup>9</sup> In 2005, for example, industry-wide expenditures in promotional activities amounted to \$18 billion (about 6% of revenues). The bulk of this came from detailing and drugs samples (Donohue et al., 2007).

<sup>10</sup> Finding a potential cooperating firm may require companies to exert effort, in the form of attending industry conferences, prepare briefings and/or hire intermediaries. This process may take up to 18 months (Agrawal et al., 2014). When a potential partner has been found, a lengthy negotiation ensues. (From our interviews with technology transfer experts, we have found out that these negotiations typically take at least 6 months can often exceed one year.)

and the associated difficulties in evaluating their technical and commercial merits (von Hippel, 1994; Pisano, 1997; Pisano, 2006; Hermosilla, 2015).

Transaction costs can be further compounded by the bargaining power asymmetry between biotech innovators and “Big Pharma” commercializers. Largely stemming from the large number of upstream innovators but small number of commercializers (Lerner and Merges, 1998; Malerba and Orsenigo, 2002; Hellman, 2007; Levine, 2009; Bosse and Alvarez, 2010), “Big Pharma” firms are usually seen as having a much stronger bargaining position than biotech firms. This prompts biotech firms to intensify their search and simultaneously negotiate with multiple firms in order to improve their bargaining position.<sup>11</sup>

In this context, the MFT will support cooperation if the total profits of doing so (net of the transaction cost) are larger than under self-commercialization. That is, if

$$D_i(1 + V_i M_{ij}) - C > D_i$$

Or equivalently, if

$$D_i > \frac{C}{V_i M_{ij}}$$

This expression illustrates that in this context, a higher demand shock always favors cooperation over self-commercialization, except for the cases in which all cooperation value is destroyed by  $V_i = 0$  or  $M_{ij} = 0$ . The expression also shows that cooperation is only viable if transaction costs are relatively low with respect to the value of cooperation,  $V_i M_{ij}$ . Heterogeneity in  $M_{ij}$  warrants that at any non-zeros  $V_i$ , some cooperation will fail due to poor matches.

Assuming a mass of technologies equal to 1 and conditional on the value of transaction costs, the total number of cooperation agreements in the  $(V_i, D_i)$  is given by

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<sup>11</sup> As in Gans et al. (2002,2008), we envision the transaction cost as an independent friction to that caused by imperfect intellectual property rights. One reason for this is that, as opposed to search and negotiation, there is not much scope for firms’ effort in accelerating the grant of patents or broadening the extent and scope their IPR protection. Both upstream and downstream firms may be reluctant to engage in negotiations before patent rights have been granted, the former fearing the risk of expropriation, the latter facing massive uncertainty about the compound’s commercial value. A second reason is that over 60% of the licensing deals observed in our sample occur after compounds have been entered to clinical trials, a stage at which compounds’ patent portfolios have usually been consolidated (Mossinghoff, 1999; Thomas, 2004; Patrick, 2013). Thus, whatever effects on licensing activity we identify are likely to stem from frictions other than the imperfections of IP protection.

$$L(V_i, D_i | C) = \begin{cases} f^V(V_i) \int_{\frac{C}{V_i D_i}}^1 f^M(M) dM & \text{if } \frac{C}{D_i} \leq V_i \\ 0 & \text{if } \frac{C}{D_i} > V_i \end{cases}$$

This expression illustrates the notion that transaction costs completely preclude cooperation for the set of technologies in the set  $\{i: D_i V_i < C\}$ . For these, even under a perfect match, transaction costs outweigh the potential gains of collaborative commercialization. For the rest, the extent of cooperation depends on both the frequency of  $V_i$  and the extent to which lower matching values will erode the gains of cooperation.

A downstream demand shock  $\theta > 0$  increases the extent of cooperation –it generates a *cooperation response*– with two mechanisms. An *intensity* effect arises among the technologies in the set  $\{i: D_i V_i \geq C\}$  (i.e., those for which cooperation was not completely precluded at the baseline demand level), as the higher demand level lowers the threshold at which an imperfect match is able to articulate cooperation. A *coverage effect* arises among technologies in the set  $\{i: D_i V_i < C\}$  as the demand shock makes cooperation viable for technologies lower in the domain of  $V$ .

These effects are illustrated by figure 3. The area below the solid curve reflects the extent of cooperation (i.e., number of cooperation agreements) at the baseline demand level. A demand shock shifts this curve outwards, increasing the extent of cooperation. The higher number of deals for technologies in the set  $\{i: D_i V_i \geq C\}$  reflected by the area between the curves entails the intensity effect. The higher number of deals associated technologies in the set  $\{i: C \geq D_i(1 + \theta)V_i, C < D_i V_i\}$  reflected by the area below the dashed curve reflects the coverage effect.

The intensity and coverage effect add up to determine the cooperation response for type  $V$  technologies. We formally define the cooperation response ( $CR$ ) as the incremental number of cooperation agreements induced by the demand shock, that is,  $CR(V_i, D_i, \theta, C) = L(V_i, D_i + \theta, C) - L(V_i, D_i, C)$ , or

$$CR(V_i, D_i, \theta, C) = \begin{cases} f^V(V_i) \int_{\frac{c}{V_i(D_i+\theta)}}^{\frac{C}{V_i D_i}} f^M(M) dM & \text{if } \frac{C}{D_i} \leq V_i \\ f^V(V_i) \int_{\frac{c}{V_i(D_i+\theta)}}^1 f^M(M) dM & \text{if } \frac{C}{D_i + \theta} \leq V_i < \frac{C}{D_i} \\ 0 & \text{if } \frac{C}{D_i + \theta} > V_i \end{cases}$$

The first case reflects the intensity effect; the second, the coverage effect. The third case points to those technologies that are excluded from cooperation even after the demand shock arrives (as its magnitude is not enough to offset  $C$  even under the perfect match) and therefore do not produce a cooperation response. It is straightforward to note that the coverage effect can only arise if  $C > 0$ , as otherwise cooperation would occur at all levels of  $V$  at the baseline demand level.

The essence of our empirical analysis is to contrast this formulation against its empirical counterpart to make an inference over the magnitude of transaction costs. If these are relatively high, the kink introduced by the coverage effect will arise towards the upper end of the distribution of  $V$ . To the left of it, the cooperation response will be null. In contrast, if transaction costs were relatively low, the kink will appear at lower ranges of  $V$ .

These patterns are crystalized by figure 4. It shows that the shape of the cooperation response across the domain of  $V$  has markedly different patterns depending on the magnitude of transaction costs. We generate this graph assuming that  $V$  and  $M$  are uniformly distributed and compare several cases, assuming different values of  $C$  (as a share of baseline demand). Consistent with our analysis, when transaction costs are null, there is no cooperation response. When these are positive but small (10% of  $D$ ), the effect is concentrated in lower ranges of  $V$  (i.e., the bottom quartile if one were to assume a uniform  $F^V$ ), as these are the technologies that were inframarginal at the baseline demand level. After this, it exhibits a downward slope. The larger transaction costs are, the larger the  $V$  value of inframarginal technologies at the baseline demand level is, hence the more intensively the cooperation response draws from higher ranges of the  $V$  distribution.

## 2.2 Empirical Strategy

We denote by  $N_V^t$  the total number of technologies (i.e., compounds) with associated to cooperation value  $V$  that are eligible for cooperation on period  $t$ , where  $t < t^*$  represents the periods before the demand shock arrives and  $t \geq t^*$  those in which the demand shock is in place. There are two types of compounds,  $k = 1$  (no exposure to the demand shock) and  $k = 2$  (exposed to the demand shock). The number of newly signed cooperation agreements is  $L_V^{tk}$ . The empirical counterpart of the probability of cooperation in the cell  $(t, k, V)$  is

$$\Pr(\text{coop}|t, k, V) = \frac{L_V^{tk}}{\alpha_V^{tk} N_V^t}$$

where  $\alpha_V^{tk}$  represents the share of  $N_V^t$  that is type  $k$  in period  $t$ . In our data we neither observe  $\alpha_V^{tk}$  nor  $N_V^t$ , so we rely on a difference-in-difference strategy and the assumption that  $\alpha_V^{tk}$  is constant in time (i.e.,  $\alpha_V^{tk} = \alpha_V^k$ ).<sup>12</sup>

Based on our proxy for  $V$ , we estimate models with the following specification

$$L_V^{tk} = g(\beta_V^0 + \beta_V^1 \cdot \mathbf{1}[k = 2] + \beta_V^2 \cdot \mathbf{1}[k = 2] \cdot \mathbf{1}[t \geq t^*] + \delta_V^t + u_V^{tk}),$$

where  $\mathbf{1}[\cdot]$  is an indicator function,  $\delta_V^t$  are year fixed effects,  $u_V^{tk}$  is an idiosyncratic error, a  $g$  represents the functional form associated to a Poisson count model. Baseline differences in the number of compounds that are eligible for cooperation (i.e.,  $\alpha_V^k$ ) are picked up by  $\beta_V^1$ . Time fixed effects control for changes in macroeconomic conditions that may induce an overall increase (or decline) in licensing (Lerner et al., 2002). The estimated coefficient of  $\beta_V^2$  picks up the differential licensing-based cooperation between the compounds that were exposed to the demand shock and those that were not. That is,  $\beta_V^2$  identifies the cooperation response among compounds with cooperation value  $V$ . Comparing the estimates of  $\beta_V^2$  across ranges of  $V$ , and based on the patterns shown in figure 4, we can evaluate whether the anatomy of cooperation response evidenced by

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<sup>12</sup> This assumption is reasonable in the short-term as, given the characteristics of the innovative process in this industry, a supply reaction should not be immediate. Indeed, Blume-Kohout and Sood (2013) Dranove et al. (2014) have shown that these “endogenous supply” effects kicked with a lag of about 4 years, after the identified cooperation response occurred. Later we provide evidence to support this claim.

figure 2 resembled that of a market with relatively low or relatively high transaction costs.

### 3. Licensing data

Our main source of data is the Thomson Reuters Cortellis Life Sciences data, a comprehensive repository of drug licensing data. This data subscription service is widely used by industry practitioners to inform strategic development decisions and prepare for negotiations. Some subsets of the data have also been used by academics in various subfields of economics and management (Lerner and Merges, 1998; Lerner et al., 2003; Lerner and Malmendier, 2010; Dranove et al., 2014; Hermosilla, 2015).

Our main set of results is drawn from the “Recap – DEAL Builder” tool offered by the Cortellis subscription,<sup>13</sup> which tracks strategic alliance activity in the sector. Recap is known as the gold standard for actionable data on biopharmaceutical deal making, as it contains information of over 40,000 alliances struck since the early 1970s. The company obtains alliance information through Freedom of Information Act requests to the Securities and Exchange Commission (SEC). Publicly traded firms are required by law to submit this information, while privately held firms also have to in some states if they provide employees with stock option plans (Lerner and Merges, 1998). Privately held firms will also submit this information voluntarily if they aspire to become publicly traded at some point. Thus, the Recap sample presumably accounts for all deals in which at least one US-based firm is involved.

The definition of alliance is wide encompassing in this industry. It includes early-stage joint ventures, contracted research, the licensing of research tools and other auxiliary technologies, as well as collaborative development and commercialization of compounds. While all these forms of collaboration usually imply some form of licensing of intellectual property, they arise in different environments and are governed by different forces. Joint ventures tend to occur before a drug candidate is discovered, when

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<sup>13</sup> The Recap service was originally provided by a San Francisco based independent company (Recombinant Capital) and later acquired by Deloitte, which later sold it to Thomson Reuters in 2013.

two or more firms believe their expertise (or IP portfolios) could be combined to produce the defining IP for a new compound. Research tools and contracted research are typically traded in the form of services purchased by a focal innovator firm that has already defined the basic design of the compound to be developed, but needs help doing so. Similarly, auxiliary technologies (e.g., drug delivery) are licensed to enhance the design or quality of the developing compound. Thus, these three forms of collaboration tend to occur early in the development process (before the compound's main technological characteristics are defined) and are reasonably described as horizontal alliances. Indeed, a significant share of this type of alliances is signed between small biotech firms without presence in the downstream drug market.

Collaborative development and commercialization is, on the other hand, better described as a vertical alliance. In this case, an innovative firm developing a compound with an already well-defined technological core faces the commercialization dilemma, choosing between self-commercialization and cooperation with an established commercializer. On the side of the market, established commercializers are prompted to enter into these alliances in order to maintain or enhance their position in the downstream market through these outsourced innovations.

By virtue of the design of the licensing contract, innovator and commercializing firms commit to combine their expertise in order to gain regulatory approval. Control rights are shared (Lerner and Merger, 1998; Anand and Khanna, 2000; Lerner et al., 2003; Lerner and Malmendier, 2010) and profits too, through milestone payments and royalties on revenues (Allain et al., 2011; Giovanetti and Jaggi, 2012; Hermosilla, 2015). This type of deals is typically referred to as a “strategic alliance” because, by agreeing to a licensing contract, firms engage in a medium to long-term collaboration.

Our main analysis focuses on development and commercialization collaborations, as measured by the number of what the data reports as new “development and commercialization” and “commercialization” licensing contracts signed each year. There are 12,846 of these contracts in the data. As opposed to the other types of collaboration agreements, these deals always entail a relatively well-defined compound. That is, these

deals trade the commercialization rights for a narrow-focused core technological component from which a final product (a pharmaceutical drug) is developed.<sup>14</sup>

Licensing deals specify the set of the compound's therapeutical applications (“indications”) for which commercialization rights are granted. This feature is essential for our empirical strategy, as it allows us to create a link between each compound and its degree of exposure to the downstream demand shock implied by Part D. In defining our sample, we drop the 3,408 deals for which the list of licensed indications is or contains missing data and the 1,866 for which we were not able to match to the MMS variable across all indications.<sup>15</sup> Finally, we restrict the period of analysis to 1995-2014, which leaves us with a total of 7,224 licensing contracts in the analyzed sample.

Because Part D impacted the demand of US consumers only, we differentiate between the deals that included the US in the licensed territories and those that did not. A deal is coded as including US territories if the “Included Territories” variable in the data contains “US,” “Nafta,” “North America,” or “World” and the “Excluded territories” variable does not contain “US,” “Nafta,” or “North America.”<sup>16</sup> Over two thirds of the contracts coded as including the US territory provide worldwide commercialization rights. This suggests that our measurement of the cooperation response will be subject to an attenuation bias, since only a subset of the populations included in the territories covered by the commercialization rights in these contracts had their demand boosted by the passage of Part D.

Table 1 presents descriptive statistics. A first observation is that most contracts in our sample (71%) do not include the US territory. We interpret this as a sign of firms' heterogeneous competitive advantages across markets (Kyle, 2006). For example, the

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<sup>14</sup> Yet another type of collaboration can occur through mergers and acquisitions (Gans et al., 2002; Higgins and Rodriguez, 2006). We do not account for these in our analysis since our focus resides on the impediments to the type of arm's length cooperation enabled by MFT. We acknowledge that the licensing and M&As markets are likely to be interconnected, but note that excluding M&A activity from our analysis could only introduce an attenuation bias on the identified effect of Part D on cooperation patterns.

<sup>15</sup> We describe the matching procedure in section 5.

<sup>16</sup> There is a highly significant although small correlation (0.23) between the dichotomic variable that indicates whether the licensing deal includes the US and that which indicates whether the in-licensing firm has headquarters located in the US. This is a reflection of the fact that many foreign companies (e.g., Novartis, Sanofi, Takeda) commercialize drugs in the US. Despite this low correlation, all our results remain qualitatively unaffected when we consider the location of the in-licensing firm's headquarters instead of the inclusion of US territories.

capabilities required to commercialize compounds in Asia may be different to those required for South America or Africa, implying that more than one deal will typically be observed to allocate a compound's ex-US commercialization rights.

## 4. Number of prescribing physicians and the value of cooperation

Here we describe the construction of our proxy value of cooperation --a compound's number of prescribing physicians (NPP). We then describe the construction of a sample used to validate its use, and provide results that demonstrate the variable's adequacy.

### 4.1 Number of prescribing physicians

As per our arguments in section 2, this variable should reflect the magnitude of investment in sales force development required for self-commercialization. We obtained the number of active physicians by specialty from the Association of American Medical Colleges "Physician Specialty Data Book" (Association of American Medical Colleges, 2012). This source lists 36 specialties with their respective number of physicians actively providing patient care in the US (as of 2012). The mean number of physicians per specialty is about 17,000. Its high standard deviation (over 22,000) is largely driven by two outlier categories, general practice/family medicine and internal medicine, each of which has over 90,000 active physicians, and to which we refer to as "non-specialists." We then asked an expert to generate a mapping between targeted conditions and physician specialties that are likely to prescribe treatments for each of them. The average number of specialties per indication was 3.2 (median 3), the standard deviation, 1.2, and the maximum 7. Using this indication/specialty mapping, we identified the set of unique specialties associated to each compound and computed NPP by summing up the total number of physicians associated to each of the specialties in this set. That is, if a

compound contains two or more indications associated to the same specialty, we only count that specialties' number of physicians once.<sup>17</sup>

The large number non-specialist physicians, fundamental ambiguity and data limitations introduce some inaccuracies to this procedure. The main problem is that for most targeted conditions it is possible to imagine a situation in which a non-specialist could write prescriptions.<sup>18</sup> Data limitations play in because targeted conditions are reported broadly. For example, depending on the severity of the injury, a non-specialist or dermatologist could prescribe a drug to treat skin burns. However, data only report the targeted indication as “skin burns” without qualifying its degree. Fundamental ambiguity exists because for many conditions, both specialists and non-specialists may be prescribers. Take for example the case of diabetes. If an individual seeks treatment because she starts to feel symptoms or the disease suddenly unravels, it is more likely that a non-specialist will provide initial prescriptions. An endocrinologist, who will prescribe a more definitive treatment, will at some point, evaluate this patient. After this occurs, many times a non-specialist will handle follow up visits and refills.

In our view, computing the NPP variable including non-specialties introduces misleading variation. This is because for multiple-indication compounds (53% and 34% in the pipelines and deals samples, respectively) the probabilities of including one or both non-specialist categories strongly increase with the number of indications, so that each compound's number of indications largely drives the resulting NPP distribution. We will therefore primarily rely on the variation of the NPP variable constructed without considering non-specialist physicians. Our analysis in the next section validates this variable as a proxy for the value of cooperation (a relationship that still holds for the version of the variable that includes non-specialists).

Figure 3 presents the Kernel distributions of the NPP variable (specialists only) used in for our main set of results. The distributions for the compounds in the licensing

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<sup>17</sup> To clarify this, consider the following example. Suppose a compound has two indications. One of these is prescribed by cardiologists (with total number of active physicians equals to  $N_c$ ) and psychiatrists ( $N_p$ ); the other, by cardiologists and gastroenterologists ( $N_g$ ). The NPP value for this compound is computed as  $N_c+N_p+N_g$ .

<sup>18</sup> In the constructed mapping, 55% of targeted conditions are coded as having medicines prescribed by internists, 79% by general practice/family medicine, and only 13% by specialties other than these two.

deals and pipelines data (described next) are overall very similar, although the former presents a slight first order stochastic dominance.<sup>19</sup> Consequently, the median NPP for compounds in the pipeline data is larger (43,000 vs 39,000). Later we will illustrate another important feature the variability in NPP, namely that it is large and similar across groups of compounds with different exposure to the demand shock.

## 4.2 Cortellis pipelines data

Thomson Reuters Cortellis “Competitive Intelligence” data tracks pharmaceutical drug pipelines (clinical trials, development terminations) of broad set of firms in the industry. While an absolute claim cannot be made, the data are thought to account for virtually all compounds that reach pre-clinical development.<sup>20</sup> This is reflected by the large number of compounds covered by the sample, over 55,000 by late 2014.

For each compound we observe the list of tested indications and thus are able to apply the methodology described above and construct the NPP variable. We also observe whether each compound has been subject of cooperation in the form of a “development and commercialization” or “commercialization” licensing agreement. 41% in the compounds are subject of cooperation agreements.

An important disadvantage of the data set is that compounds cannot be systematically linked to the licensing deal data, which means that we don’t observe when the cooperation agreement was struck or whether it includes the US territory. This shortcoming leaves us unable to directly test for the probability that a compound will be licensed after Part D and forces us to adopt the identification strategy laid out before, which relies on the number of observed deals. Nevertheless, by allowing us to correlate NPP with the probability that a compound will be licensed (at any given time), the pipelines data contains valuable information.

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<sup>19</sup> This is likely due to the fact that licensing deals do not always provide commercialization rights for all developing indications.

<sup>20</sup> The company collects information from a wide variety of sources (clinicaltrials.gov and international counterparts, press releases, scientific articles, conference reports, company websites, industry newsletters, grant making bodies, among others). In private email communications with firm representatives, it has been stated that the sample aims to be as comprehensive as possible. All data is manually curated (by an editorial staff of about 500) and six-sigma methodologies employed for quality control.

We restrict the sample to compounds tested on clinical trials with human subjects before 2014.<sup>21</sup> Since most of the compounds never reach clinical trials (or have not yet done so in the sample), this reduces the sample size to a total of 11,179 compounds. While some of these compounds have been discontinued or withdrawn from clinical development, their highest achieved development stage before discontinuation or market launch is reported. We code this into phase I (28%), phase II (37%), phase III (15%), and launched (20%).<sup>22</sup> We also observe the identity of the originator firm (i.e., the firm responsible for the compound's discovery), which we use to construct an indicator for the innovator firm's (lack of) market presence. Firms are deemed as having no market presence if none of their originated compounds has been self-commercialized (i.e., commercialized without cooperation).<sup>23</sup> This definition works well for compounds reaching highest stages in clinical trials, but inhibits inference over the extent of cooperation for those compounds that reach the market (since, by definition, the probability of cooperation would be zero). Therefore, in this case, firms without market presence are defined as those having originated exactly one commercialized compound. With this definition, 63% of compounds in the sample are originated within firms without market presence.

### 4.3 Validation

As explained before, the sample corresponds to a snapshot of compounds registering clinical trial activity in 1995-2014. We produce two important findings: (i) NPP is strongly correlated with the probability of cooperation, and (ii) the probability of

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<sup>21</sup> We do not consider phase IV clinical trials, which are conducted after launch.

<sup>22</sup> The original data set reports a noisy and incomplete variable. Its noise seems to be originated on clinical trial progress that has not yet been incorporated. Its incompleteness, from the fact that the highest achieved development stage is not reported for withdrawn compounds. We correct these problems by bringing in clinical trial data. In the used coding phase I includes reported "phase 1," "phase 1a," and "phase 1b" entries. Phase 2 includes "phase 1/phase 2," "phase 2," "phase 2a," and "phase 2b." Phase 3 includes "phase 2/phase 3," "phase 3," "phase 3a," and "phase 3b." We also code as having reached phase 3 those compounds that reach the FDA pre-registration or registration stage (these correspond to less than 2% of all compounds coded as reaching phase 3).

<sup>23</sup> Results do not significantly change when we instead define no market presence as having no commercialized compound at all (i.e., with or without cooperation).

cooperation is generally high, particularly for innovator firms without presence in the downstream market.

Table 2 presents the probability of cooperation and number of compounds reaching different stages, by NPP quartile (NPP does not include non-specialists). This probability is computed as the mean of a dichotomic variable that equals 1 if a compound registers a cooperation agreement (and 0 otherwise) within each NPP quartile/stage cell. We present results for the whole sample of compounds (panel A) and also for a subsample of compounds originated in firms without market presence (panel B). Making this distinction allows us to control for the fact some innovators (those with market presence) may have in place distribution channels and other assets required for commercialization.

The probability of cooperation increases both with the highest achieved stage and NPP. This finding is robust across subsamples (firms with and without market presence). The slopes across subsamples are similar, but baseline probabilities of cooperation are higher for firms without market presence. For firms lacking market presence self-commercialization implies a sunk cost associated generating brand recognition, and assembling and training a sales force. For firms with market presence, brand recognition and an assembled sales force may be in place, but additional marketing activities, re-training or additional hiring may be required if novel compounds target a different physician population. Overall, for compounds that have been launched, the probability of cooperation is 0.62 in the lowest NPP quartile and 0.74 in the highest quartile. For compounds originated within firms without market presence, these probabilities are respectively 0.66 and 0.78.

Estimates from linear probability models presented in table 3 (panel A) estimated on stage-specific samples crystallize these patterns. As reflected by the models' constants, baseline cooperation probabilities increase throughout stages, with particularly large increases at the two higher stages. The significant increase in the baseline probability of cooperation from phase I to phase II may be justified by the relative complexity of the latter type of trials (Danzon et al., 2005), but also the fact that phase II "proof of concept" trials are usually considered pivotal, therefore reducing the amount of uncertainty

regarding the probability of obtaining regulatory approval and facilitating negotiations. As argued by Hermosilla (2015), this is also consistent with strategic time-to-license decisions by biotech firms who anticipate more attractive licensing contracts at late development stages. A further reduction in uncertainty may underlie the even larger increase in the baseline probability of cooperation observed from phase III to launched compounds.

From the point of view of our analysis, the main result is the systematic and highly significant positive correlation between NPP and the probability of cooperation.<sup>24</sup> This result holds even after controlling for firms' market presence, suggesting that the commercialization of each new compound implies additional investment in distribution channels. For compounds that reach Phase II of clinical trials, the estimate suggests that increasing the number of prescribing physicians one standard deviation increases the probability of cooperation by about 7 points. We believe that this evidence supports the validity of NPP as a proxy for the *intrinsic value of cooperation* ( $v$ ).

Panel B of table 3 corroborates this conclusion with estimates obtained with the NPP variable that includes non-specialist physicians. Aside from the obvious differences caused by the different scaling of variables, estimates are very similar. This is comforting in that it suggests that inaccuracies in the computation of the NPP variable should not severely damage its informational content. Due to the high number of indications coded in our data as prescribed by non-specialists (87%), we believe that the version of the NPP variable which does not include non-specialists is a more reliable proxy for the intrinsic value of cooperation. Hence, this is the version we use in the remainder of our analysis.

## 5. Medicare Part D

### 5.1 The Program

Medicare is an important social insurance program in the United States, providing medical insurance primarily for the elderly (65 years and older) and disabled. Since its

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<sup>24</sup> This result also holds true in the estimates of (unreported) models that do not account for market presence.

creation in 1965, Medicare has covered beneficiaries' inpatient and outpatient expenditure through Medicare Part A and Part B, but offered little prescription drug coverage until recently. In December 2003, Medicare Part D was enacted as part of the Medicare Modernization Act to provide outpatient prescription drug insurance to Medicare beneficiaries. The program was implemented in January 1, 2006.

Part D is a large-scale program, both in terms of the number of enrollees and its cost. In 2006, there were 26 million Medicare beneficiaries enrolled in Part D. The annual program cost was about 50 billion in 2008 and about 63 billion in 2012, implying that the average expenditure per-patient was close to \$2,000 in 2008. The Congressional Budget Office (2014) predicts that the total program costs will grow to \$76 billion by 2015.

By various accounts, Part D was a significant shock to the industry. Blume-Kohout and Sood (2013) and Dranove et al. (2014) find the program incentivized the innovation of more prescription drugs targeting the conditions that are more prevalent among enrollees.<sup>25</sup> The program was also found to have increased prescription drug usage among enrollees by between 4.7% and 5.9% (Ketcham and Simon, 2008; Yin et al., 2008).<sup>26</sup>

It is possible that some of compounds in deal data were not meant to be commercialized as prescription drugs but instead be used for in-patient care. These types of treatments are usually not covered by Part D, but by Part B. This suggests that our empirical estimate of the cooperation response to the program may be affected by an attenuation bias. However, as discussed by Dranove et al. (2014), Part D provided coverage for many drugs used for in-patient treatments, including many of the top-selling biologic cancer treatments in 2009-2012.

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<sup>25</sup> Later we will address the possibility that these endogenous supply effects could confound our inference.

<sup>26</sup> Unlike traditional government-sponsored programs, the benefits entailed Part D are delivered to Medicare enrollees by private insurance companies. These firms design formularies (i.e., coverage plans), which specify the magnitude and breadth of prescription drug coverage. Consumers then choose among these plans. The government, represented by Center for Medicare and Medicaid Services (CMS), limits its role to setting up basic guidelines and is prohibited by law from directly bargaining with pharmaceutical firms.

## 5.2 Sizing Part D's Demand Shock

In order to size the magnitude of the demand shock posed by Part D across therapeutical categories, we adopt the approach of previous research (Duggan and Scott-Morton, 2010; Blume-Kohut and Sood, 2013; Dranove et al., 2014) by creating a variable that measures the extent to which expenditure on a given drug is expected to come from prescriptions issued to Medicare enrollees. As in these previous papers, we label this variable “Medicare Market Share” (MMS).

To construct this variable we utilize data from the Medical Expenditure Panel Survey (MEPS),<sup>27</sup> a large, representative sample of US individuals' medical service utilization, including suffered conditions and the availability and type of insurance. Using the 2003 MEPS insurance and conditions files, we compute MMS as the percentage of individuals that suffer a particular condition that are Medicare enrollees. Thus, the domain of MMS is the unitary interval and a value of 0.5 for a specific condition indicates that 50% of the population suffering that condition in 2003 was enrolled in Medicare during that same year.

A limitation of the MEPS data is that specific conditions suffered by each individual are not reported by their name or coded granularly. Instead, they are reported by their corresponding ICD-9 therapeutic category. The International Statistical Classification of Diseases and Related Health Problems (ICD) is a widely used therapeutical classification system maintained by the World Health Organization and used to monitor worldwide morbidity and mortality statistics, aid in reimbursement processes and automated decision support in healthcare.<sup>28</sup> At its most granular level, the ICD9 system achieves a great deal of precision. However, MEPS reports conditions are reported at their least granular level, which has about 800 broad therapeutical categories. We thus bridge indications in our data to MEPS insurance variability at this level.

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<sup>27</sup> MEPS data are available for download at <http://meps.ahrq.gov/mepsweb/>.

<sup>28</sup> About 70% of worldwide expenditure is allocated using this system for reimbursement. <http://www.who.int/classifications/icd/en/>

Indications in the deal data cover 284 of such categories, with an average of 2.75 conditions per category.

Figure 6 presents the kernel distribution of MMS scores across indications associated to the compounds in the licensing data. Overall, there is substantial heterogeneity and patterns of variation result fairly intuitive as the epidemiological characteristics of conditions with high MMS scores are those one would associate with Medicare enrollees (i.e., 65 years and above). For example, at the bottom of the distribution, with MMS scores below 0.1, we observe conditions like growth hormone deficiency, attention deficit disorder and acne. With MMS scores between 0.2 and 0.3 there are, for example, conditions like myopia and psoriasis. More Medicare-oriented diseases include hyperlipidemia, chronic bronchitis and hypertension (MMS between 0.4 and 0.5). At the top of the distribution there are conditions like cardiac failure, cataracts, Alzheimer's and Parkinson's disease (all with MMS scores above 0.8), which are typically suffered by relatively older people. The median of this distribution is 0.32.

Licensing deals typically stipulate the rights to commercialize a multiple indications of a single compound. In our data, this is the case for 82% of deals, with an average number of 1.7 licensed indications per deal and a standard deviation of 1.5. In rigour, a compound's exposure to the Part D shock depends on all of the covered indication's individual MMS scores, weighed by a function of their individual stage of development at licensing (as a proxy for the probability of obtaining regulatory approval). Our data, however, only provides information about the highest stage of development at licensing among all included indications. We thus base our empirical analysis on the dichotomic variable DMMS, which equals 1 at least one above-median MMS indication is licensed, and zero otherwise. This definition implies that DMMS=1 compounds were relatively more exposed to the demand shock than DMMS=0 compounds. While there is within-deal MMS heterogeneity, most variability (60%) arises at the between-deal level, implying that this aggregation remains informative. This said, we acknowledge that this coding may introduce an attenuation bias. We accept this inferential cost because this procedure greatly simplifies the analysis, but also because our main interest resides on identifying the cooperation response rather than implementing an accurate measurement. In the remainder of the analysis we will

interchangeably use “DMMS=1” deals with “Medicare-oriented” deals and “high (demand shock) exposure” deals.

An important feature of the data is the joint variability of DMMS and NPP. Our discussion above presented NPP as a proxy for the intrinsic value of cooperation, a driver of the scaled value of cooperation that operates through mechanisms other than downstream demand. In order to locate the cooperation response along the distribution of cooperation values, it is required for DMMS to offer variation across NPP levels. The raw correlation between the variables is low, at about 0.11. Moreover, at all levels of NPP there is substantial heterogeneity in DMMS. This is illustrated by table 4, which shows that the percentage of DMMS=1 deals across quartiles of NPP range between 54% and 84%. Patterns of variation across quartiles are moreover similar for deals including and not including US territories.

Finally, the variation of DMMS and NPP seems to be largely independent from each compound’s baseline demand. We evaluate this patterns using additional data from the 2003 MEPS survey: total number of patients, total number of prescriptions and total expenditure in prescription drugs.<sup>29</sup> Table 5 presents the correlations of the MMS and NPP<sup>30</sup> variables with each of these proxies. These correlations are occasionally significant at conventional confidence levels, but in every case very close to zero. Figures 5a and 5b further show wide dispersion of each of these variables at all levels of MMS and NPP. This evidence is consistent with our independence assumptions of section 2.2. Nevertheless, we recognize that unaccounted determinants of market potential (such as number of competitors) may be relevant, introducing a degree of unobserved correlation.

## 6. The Cooperation Response

Figure 1 evidenced our main results, a strong, short-termed licensing response in the drug licensing market fueled by the downstream demand shock entailed by Part D. In

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<sup>29</sup> All variables are at the ICD9 integer level. Includes all individuals in the 2003 MEPS data (i.e., enrollees and non-enrollees of Medicare).

<sup>30</sup> As opposed to the rest of our analysis, in this case with consider the number of prescribing physicians at the indication level. Does not include non-specialists.

this section we present further evidence, which corroborates statistically and further explore the nature of the effect.

## 6.1 Main effects

We start by analyzing the trends in the number of deals including and not including the US. Table 6 breaks down the yearly average number of deals by time periods and DMMS. Drawing from the trends in figure 1.1, we break down the 20 years of data into three periods: 1995-2003 (period 1), 2004-2010 (period 2), and 2011-2014 (period 3).

The number of DMMS=1 deals is systematically larger than that of DMMS=0 (by a factor of about 2). The stability of this relationship across time periods is more notorious among deals that do not include the US, which lends support our identification assumption of a constant  $\alpha$ . The greater proportion of DMMS=1 deals arises in part due to the construction of the variable<sup>31</sup> but also as a reflection of upstream innovators' relative focus on cancer treatments, which is more frequently observed among older individuals.<sup>32</sup> Our econometric specifications below will capture this effect by including DMMS as an independent variable.

In period 2, immediately following the enactment of Part D, the average number of DMMS=1 deals including the US increased by 73%, much more than the growth in the average number of DMMS=0 deals (44%) including the US. This difference is consistent with a cooperation response unfolding between 2004 and 2010. After 2010, in period 3, the average number of each type of deal returned to levels close to the ones originally observed in period 1.

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<sup>31</sup> To see this, recall that DMMS equals one if at least one of the compound's indications has an above-median MMS score. For single indication compounds, the probability of DMMS=1 equals the probability that the single indication will have an above-median score, that is, 0.5. For multiple indication compounds, however, the probability of DMMS=1 equals the sum of the probability that each of the compound's indications will have an above-median score. As we mentioned earlier, 82% of the licensing deals contain more than one indication implying a higher baseline higher probability of DMMS=1 than DMMS=0.

<sup>32</sup> Other studies analyzing patterns in drug development (Giovanetti and Jaggi, 2012; Dranove et al., 2014) show that about half of indications originated in biotech firms and entered to clinical trial development target a cancer condition.

A relative increase in the period 2 average number of DMMS=1 deals also occurred among agreements not including commercialization in the US. This difference was, however, much smaller than for deals including the US. A higher baseline increase of US deals is justified because Part D also affected DMMS=0 deals (as their indications are associated to positive MMS values), so that the relevant comparison is the relative difference between the licensing activity of DMMS=1 and DMMS=0 deals, for deals that include and do not include the US. For deals not including the US, this difference was much smaller.

Contrary to the patterns observed for deals including the US, the number of deals not including the US did not return to the original pre-2003 levels. The average number of DMMS=0 not including the US continued its period 2 expansion (almost 30% than in period 1), while and that of DMMS=1 deals slightly contracted with respect to period 2, remaining at almost 120% the level of period 1. It is hard to provide a conclusive interpretation of this phenomenon. One possibility is that the 2008 subprime crisis impacted upstream innovators around the world with different intensities and at different times. Lerner et al. (2002) show that the availability of financing from public investment markets may condition the structure of financing of biotech firms. Facing a depressed equity financing market after the 2008 subprime crisis, biotech firms may have increased the reliance of licensing-based financing. Time differentiated effects across local financing markets around the world and the higher participation of ex-US out-licensors in deals not including the US,<sup>33</sup> may thus have configured these trends.

Estimates presented in table 7 are derived from Poisson count models with robust standard errors. The dependent variable is in column 1 aggregates the number of deals including the US; those of column 2, deals not including the US. In both cases, deals are aggregated within each year/DMMS cell. Thus, because we have a 20-year sample, models are estimated each with 40 observations. The dependent variables include the dichotomic DMMS indicator, as well as its interactions with the PERIOD2 and PERIOD3 indicators. The latter variables are individually omitted because models

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<sup>33</sup> Across time periods, the participation of US and ex-US out-licensors in deals including the US is approximately even. For deals not including the US, the participation of each type of out-licensor is higher (60%) for ex-US out-licensors during periods 2 and 3.

include year specific fixed effects, which capture the potential confounding effects of varying macroeconomic conditions.

The estimated coefficient associated to DMMS quantifies the baseline licensing propensities between the compounds that contain an above-median MMS indication and those that do not. The estimated coefficient is similar across samples, in both cases positive and statistically significant at a 99% confidence level.

The magnitude of the cooperation response is given by the coefficient associated to the interactions of DMMS with PERIOD2 and PERIOD3. For compounds including the US, the interaction with PERIOD2 is positive and significant at the 95% confidence level. Its magnitude implies that, controlling for macroeconomic conditions, Part D caused an increase in the licensing of DMMS=1 compound of about 15% during 2004-2010. Consistent with our previous results, the interaction with PERIOD3 is smaller and not statistically significant, suggesting that the effect was limited to period 2. In contrast, for deals not including the US, there is no meaningful impact during period 2, and a relative decrease of DMMS=1 licensing during period 3.

## 6.2 Mapping the cooperation response along the distribution of cooperation values

Our model implies that there will only be a cooperation response if transaction costs are large enough with respect to the intrinsic value of cooperation. That is, if  $c/v > 0$ . Intuitively, only if transaction costs represent a meaningful fraction of the value of cooperation there will be a pool of forgone deals -the “deals not done” (Agrawal et al., 2014)- from which the cooperation response will draw.

This notion gives us an opportunity to identify the type of compounds that make up for the pool of forgone deals. In particular, to which extent do compounds associated to high  $v$ 's enter this pool? If the contribution is relatively uniform across the distribution of  $v$ , then the number of forgone deals is an unbiased indicator of the efficiency burden imposed by transaction costs. On the other hand, if low- $v$  compounds make up for most

of the pool of forgone deals, then the number of forgone deals overemphasizes this efficiency cost.

Figure 7 presents evidence suggesting that the cooperation response focused on low- $v$  compounds. We compute the relative increase in the yearly average of year deals in 2004-2010 relative to those in 1995-2003, by NPP quartile and deal type (DMMS=0,1). In 2004-2010, the yearly average number of DMMS=1 deals in the lowest quartile increased by about 160% with respect to its 1995-2003 baseline. On the other hand, DMMS=0 deals in this quartile, increase by 45% only. For compounds in the three upper quartiles, the relative increase was relatively similar across DMMS levels. That is, figure 5 suggests that the cooperation response focused exclusively on the lowest quartile of our proxy for  $v$ .

Table 8 corroborates this conclusion with estimates of our main Poisson specification, which controls for the variability in the public financing environment by including year specific fixed effects. Each column presents coefficients estimated on subsamples composed of compounds belonging to each of the NPP quartiles. Results show that the cooperation response identified earlier concentrated on compounds in the first quartile. The coefficient implies an even larger effect than that estimated before: Part D caused an increase of about 60% in the licensing of DMMS=1 compounds in the lowest quartile of the distribution of intrinsic values of cooperation. For compounds in the three upper quartiles, the effect is much smaller and not statistically significant at conventional confidence levels.

At this point it is also worthwhile to underline that our estimates of the cooperation response should be interpreted as a lower bound for the actual effect. We mentioned earlier that this attenuation bias could exist because many of the deals that include the US specify worldwide commercialization rights, but also because the DMMS aggregation washes away some variability regarding compounds' true exposure to the Part D demand shock. Another contributing factor is grounded on the results of the previous section, namely, that the cooperation response focuses on compounds undergoing clinical trials. The high attrition rate in drug development implies that a downstream demand shock should be adjusted down by the probability of obtaining

regulatory approval in order to generate an estimate of the elasticity of the probability of cooperation with respect to downstream market potential size. Considering the 0.62 estimate for compounds in the lowest NPP quartile and the various sources of attenuation bias, it could be possible for this elasticity to exceed 1.

This section's findings suggest that for 75% of compounds associated with higher intrinsic values of cooperation, there is not a meaningfully large pool of forgone deals. In other words, for these compounds transaction costs do not severely preclude valuable cooperation. As we conclude, in the next section we put this result in context and discuss its limitations and implications.

## 7. Short-term response and endogenous supply

Blume-Kohout and Sood (2013) and Dranove et al. (2014) show that Part D had an impact on the supply of compounds, inducing firms to introduce more Medicare-oriented compounds to clinical trials after 2003. In this section we investigate the extent of these potentially confounding endogenous supply effects by exploiting short-term patterns of the cooperation response.

We turn our attention to this matter because an increase in licensing activity purely driven by endogenous supply effects implies that the cooperation response (as given by our framework) did not exist. In terms of the validity of our assumptions, an endogenous supply effect would imply that a higher percentage of Medicare-oriented compounds entered the MFT after 2003. That is,  $\alpha$  decreased. Nevertheless, our results suggest that the cooperation response indeed existed, since the increase in licensing activity operated in the short-term, anticipating endogenous supply effects.

Before we examine the unfolding of increased cooperation in our data, we revisit the results of Blume-Kohout and Sood (2013) and Dranove et al. (2014). Using a large sample of developing drugs in the pharmaceutical industry (primarily focused on compounds developed in-house or in-licensed by "Big Pharma" firms) Blume-Kohout and Sood (2013, table 2) show that the endogenous supply effect did not operate until 2006. With a different sample (focusing on compounds originated on Biotech firms),

Dranove et al. (2014, table 2) obtain the same result. That is, both papers find that the increased clinical trial activity of Medicare-oriented compounds did not take place until 2006, the bulk of it occurring between 2008 and 2011. This result is not surprising given the fact that bringing new compounds or indications to clinical trials is a time-consuming procedure, which requires significant pre-clinical testing and the filing of an IND (investigative new drug) application to the FDA.

When we reproduce our the estimates of our main model (table 7, column 1) in a sample excluding licensing deals after 2005, the diff-in-diff coefficient that reflects the cooperation response remains positive and statistically significant (99% confidence), with a value that slightly exceeds that obtained in the full sample (0.17 vs 0.15). While this evidence is consistent with the existence of a cooperation response, it does not rule out that this increase in licensing activity could have been focused on “endogenously innovated” early stage compounds. To further explore this possibility, we look at the unfolding of the cooperation response for compounds in different stages of the development process.

Table 9 shows the short-term dynamics of the cooperation response. The reported statistic is computed as the ratio of the total number of licensing deals (including the US) that were signed on each year after 2003 to the number of deals signed in 2003. Thus, the second number in column 4 (1.9) means that in 2004 there were 90% more DMMS=1 licensing deals of compounds in being tested in clinical trials than there were in 2003. On the other hand, the second number of column 3 (1.2) suggests that in 2004 there were only 20% more DMMS=0 licensing deals of compounds in clinical trials than there were in 2003.

These two numbers illustrate the main result in the table. The cooperation response of compounds in clinical trials was instantaneous, preceding the endogenous supply effects identified by Blume-Kohout and Sood (2013) and Dranove et al. (2014). Relative to 2003 levels, the licensing of DMMS=1 compounds almost doubled initially and more than doubled in the years that followed. For DMMS=0 compounds in clinical trials, there was a mild initial increase in licensing, but which was later reverted. The licensing of early stage compounds (in the discovery stage, columns 1 and 2)

experimented a milder increase relative to 2003 levels, but which was less differentiated across DMMS levels. Together, the lack of short-term response in cooperation among early stage compounds and the large response among compounds in clinical trials negates the possibility that the increase in licensing activity was driven by endogenous supply effects.

The intensity of the short-term response for compounds in clinical trials further suggests that Part D may have catalyzed negotiations ongoing in 2003 by enlarging the bargaining core (Lerner et al., 2002) making it easier for firms to agree to fair terms. This bargaining core effect was presumably much smaller or null for early stage compounds since, as discussed in section 2, they usually lack consolidated patent portfolios thus making many firms reluctant to engage in negotiations. Consequently, no cooperation response was observed among compounds in the discovery stage.

In addition, the gradual increase in the cooperation over clinical trial compounds is consistent with firms intensifying search. The rate of increase of DMMS=1 licensing deals after 2004 is, however, less significant and mainly coincides with the time the endogenous supply kicked in.

Finally, we note that the lack of a cooperation response among launched compounds is consistent with lower transaction costs. After compounds are launched, uncertainty over market potential is much smaller, which is likely to greatly simplify the negotiation process. In addition, search costs are likely to be smaller, since after years of development and regulatory scrutiny, compounds' are well known by the set of potential partners. Furthermore, as suggested by Kyle (2006), there may be large gains from cooperating with local commercializing firms. In sum, for launch compounds we should expect  $c/v$  to be relatively low. As prescribed by our characterization of the cooperation response in section 2, in these cases the cooperation response will be weak, if existing at all.

## 8. Conclusions

An assessment of the literature exploring the functioning of Markets for Technology (MFT) surfaces a consensus on the idea that transaction costs may delay and hamper valuable cooperation between innovating and commercializing firms. To the best of our knowledge, this paper constitutes the first deliberate attempt to place context around the magnitude of the efficiency burden imposed by these frictions. Based on the importance of MFT to innovation and growth we believe this to be an important line of research.

We exploit the impact of the 2003 enactment of the Medicare Part D program on the drug licensing market to shed light on the matter. This program constituted a significant expansion of prescription drug coverage for Medicare enrollees, effectively increasing downstream consumer demand for drugs targeting conditions that are more prevalent among the enrolled population (65 years and older). We document a strong, short-term surge of licensing-based cooperation for the development and commercialization of pharmaceuticals targeting the therapeutical conditions that are more prevalent among the Medicare population.

Theoretically, this surge can only be rationalized if transaction costs operate in the market. This is so because only if transaction costs are large enough there will be a set of compounds for which cooperation is precluded at the baseline demand level. It is from this set that the new deals sustaining the surge in cooperation are drawn. By generating a measure for the value cooperation would add to a compounds' cooperative commercialization, we find that the increased licensing activity focused on the 25% of compounds at the bottom of this distribution, implying that transaction costs do not impede cooperation in the 75% of cases when it is most valuable. It follows that the welfare cost associated to the existence transaction costs in this market will be overestimated when measured solely by the number of "deals not done" (Agrawal et al., 2014).

The validity of this result hinges on a number of issues. One first caveat regards the quality of our proxy for the value of cooperation. We construct this measure by exploiting the variability in the magnitude of replicative investment required for self-commercialization by upstream innovators. Our analysis of cooperation patterns in a

large sample of developing compounds provides strong validation for the measure but does not rule out the possibility that the inclusion of other factors, such as those stemming from pair-wise heterogeneity in the quality of matching, could translate into a different ordering. Judging from the large importance of distribution costs in the industry (Donohue et al., 2007; Silverman, 2014) we believe that refinements to this proxy are unlikely to overturn our conclusions. Nevertheless, we think that these concerns warrant further research and in ongoing work we seek to provide more concrete evidence on the matter.

It is possible that some of the neglected cooperation at the lowest quartile of the distribution of cooperation values is self-fulfilling. Various sources have documented or referred to a degree of misalignment between the objectives of commercializing firms and those of the scientists responsible for the discovery and development of biotech compounds (Murray 2002; Gittelman and Cogut, 2003; Stern, 2004; Pisano, 2006). Therefore, it is possible that, in order to work independently, leading scientists at biotech firms choose to develop *those compounds for which self-commercialization is relatively less costly*, that is, those compounds for which investment in distribution channels is relatively small. This strategy may have become more attractive along with the rise of personalized medicine and the incentives posed by the Orphan Drug Act,<sup>34</sup> which increase the relative value of self-commercialization for compounds targeting small populations of patients. To the same extent that we give this idea some credence, we should adjust down our estimate of the efficiency burden posed by transaction costs.

The construction of our proxy for the value of cooperation also calls for a precision in the interpretation of our results. Cooperation is valuable not only because it avoids replicative investment, but also because it may exploit complementary expertise useful during the development process. These synergies could act by increasing the quality of the final product, the probability of reaching the market, or by reducing time-to-market. However, collaboration unfolds only gradually throughout stages, suggesting that these gains are not fully materialized despite their relevance in the industry. In this sense,

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<sup>34</sup> The Orphan Drug Act offers important incentives for the development of rare “orphan” diseases (i.e., less than 200,000 patients in the US). The rise of personalized medicine has prompted a subdivision of traditional definitions of diseases based on genetic-based heterogeneous responses to treatments (Yin, 2008), creating many “new” diseases that fall in the orphan category.

transaction costs are “paid” in the form of forgone benefits of complementary expertise during development. By the same logic, transaction costs are also “paid” in the form of costly and lengthy search and negotiations.

When focusing on the sample of compounds in the lowest quartile of the distribution of cooperation values (as given by our proxy), our estimates suggest that cooperation increased by about 60% for the compounds with relatively higher exposure to the demand shock. There are, however, various reasons to believe that this estimate is afflicted by an attenuation bias. This means that the elasticity of cooperation with respect to market size could well exceed unity.

While we do not explicitly model individual firm behavior, our framework is consistent with commercializing firms acting as *agents for commercialization* whose main role is to source embryonic technologies from the MFT, develop them into final products and allocate them to consumer demand. An interesting tension arises under this view. Effective commercializers would screen technologies on their expected market profitability, refraining from in-licensing those with low potential. This means that the forgone cooperation that has been typically been attributed to contracting frictions by the “supply side” literature (Arora and Gambardella, 2010) could potentially be rendered as an efficient outcome. Evaluating this hypothesis, however, requires the collection of additional and possibly tailored econometrics, which lies beyond the scope of this paper. Sharing Arora and Gambardella’s (2010) call for an increased focus on the “demand side” of MFT, we believe that further theoretical and empirical work would be useful to better understand the determinants, nuances and implications of statistics such as the elasticity of licensing to downstream market size.

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## Figures and Tables

Figure 1: Distribution of number of prescribing physicians (NPP) in the licensing data.

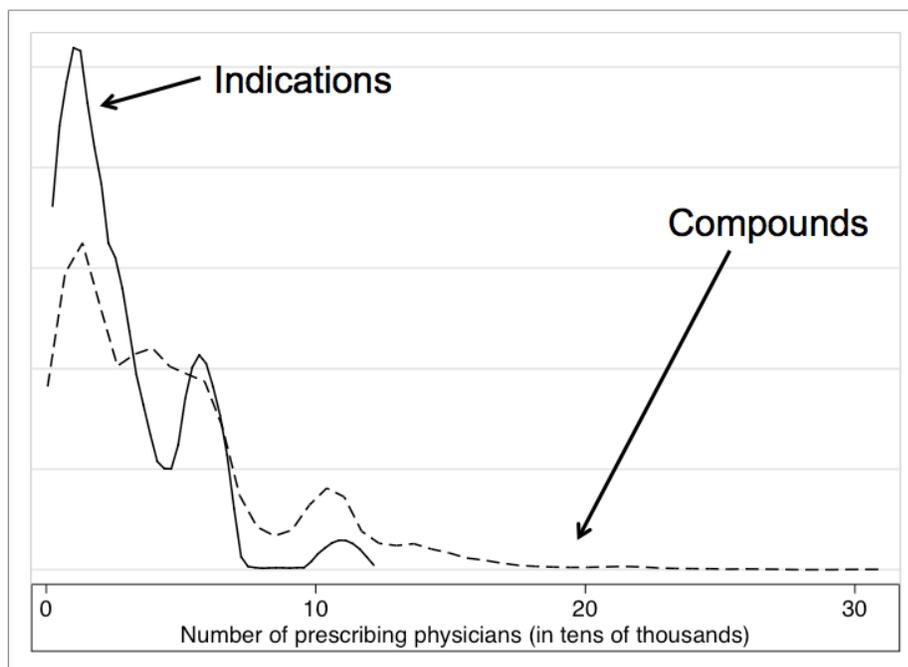


Figure 2: Number of deals including the US territory, 1995-2014

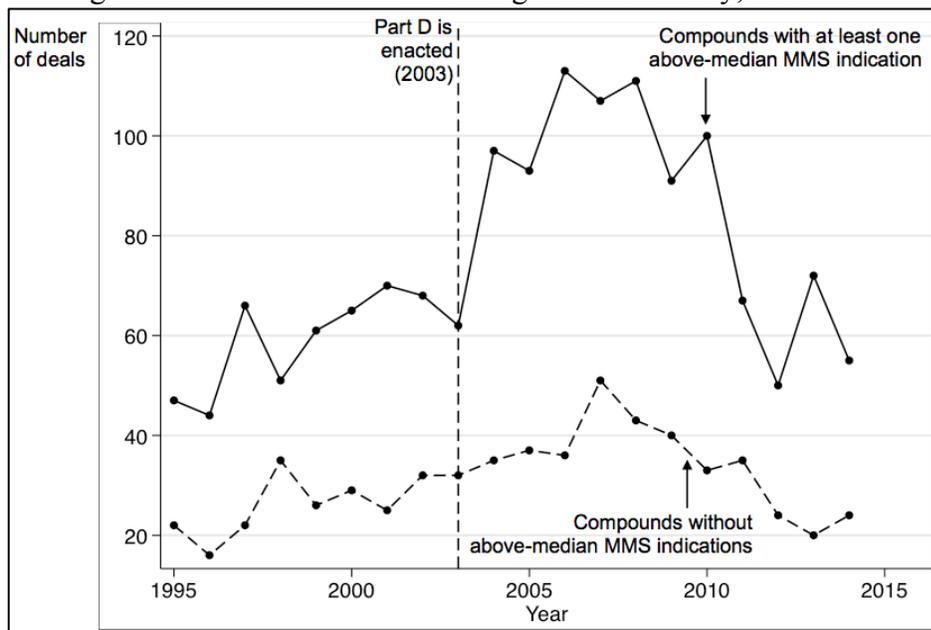


Figure 3: Number of deals not including the US territory, 1995-2014

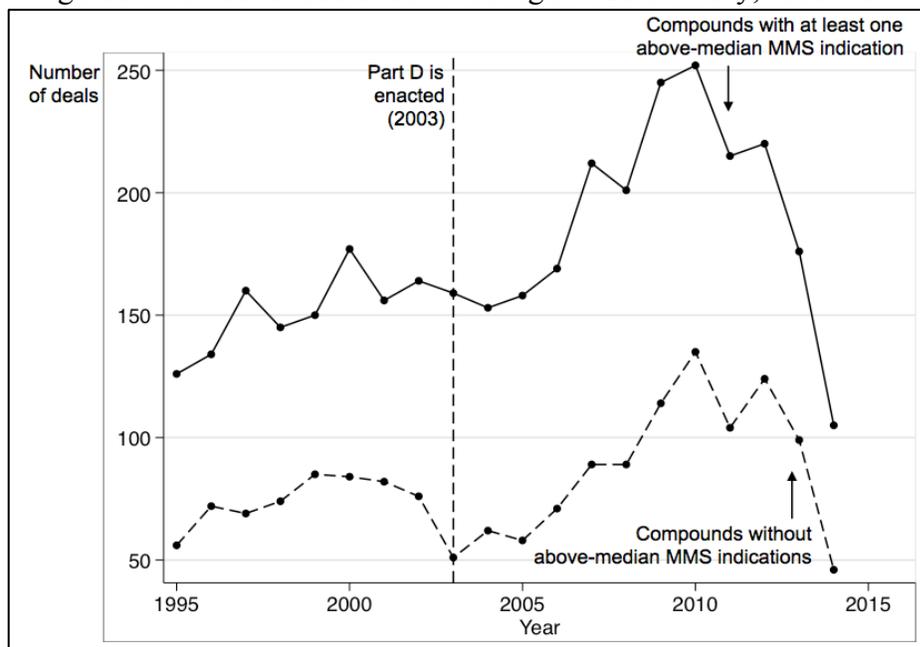


Figure 4: Intensity and coverage effects provoked by a downstream demand shock.

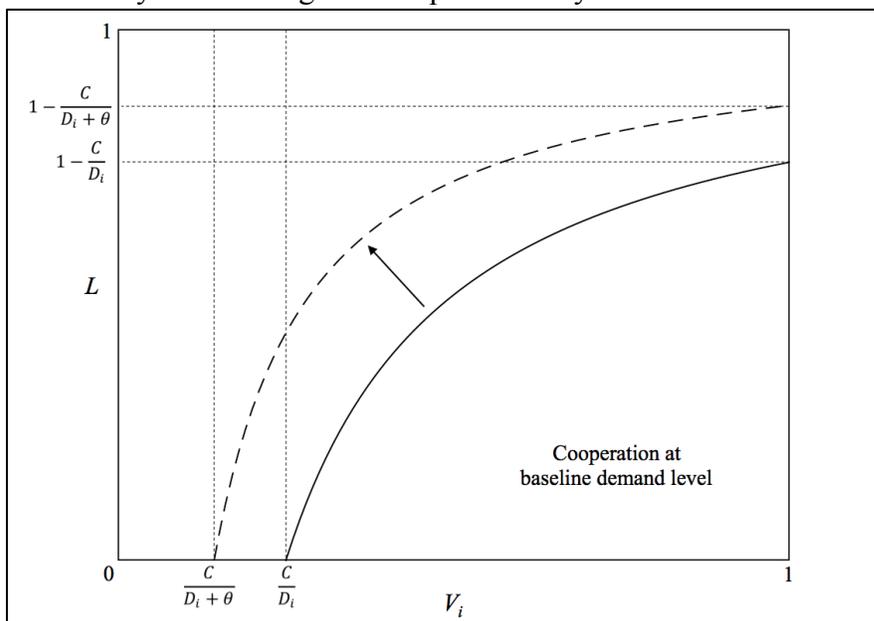
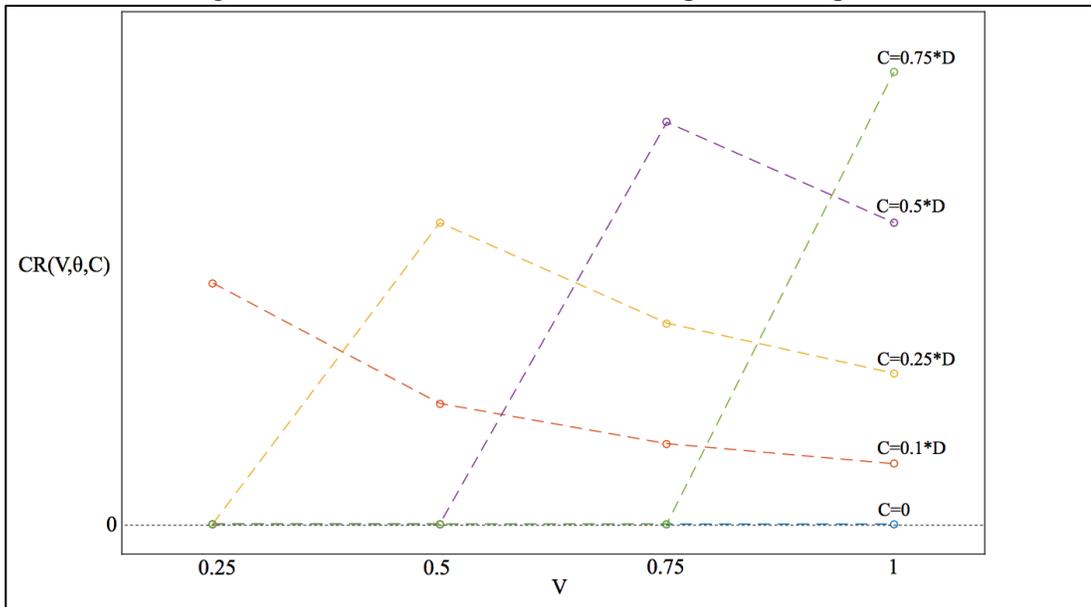


Figure 5: Transaction costs and the cooperation response.



Calibration assuming M and V uniform.

Figure 6: Kernel distribution of MMS scores for conditions targeted by compounds in the deals data. (Each observation is a unique targeted condition.)

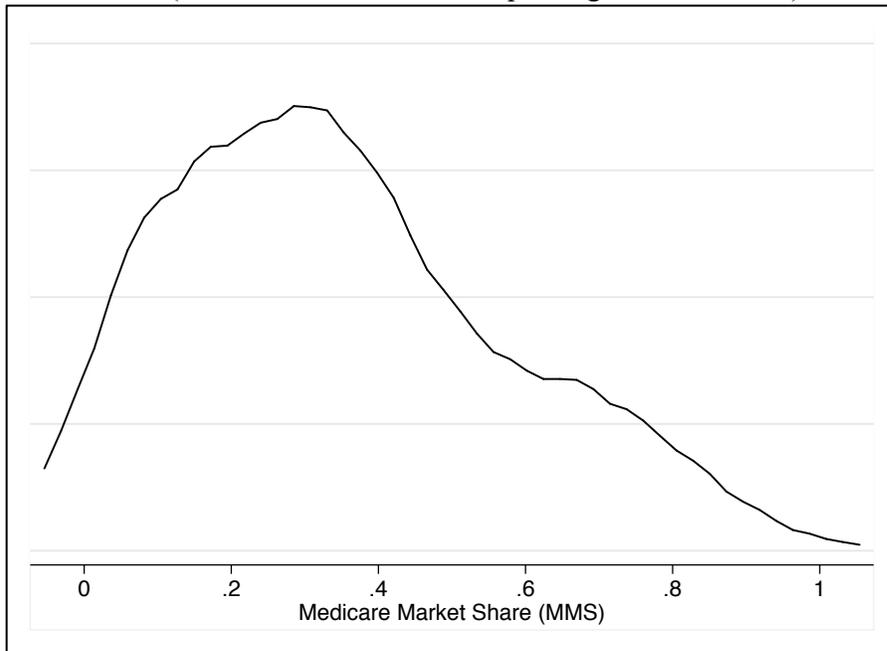


Figure 7: The cooperation response by NPP quartile. (Computed as percentage increases in total number of deals including the US: 2004-2010 vs 1995-2003)

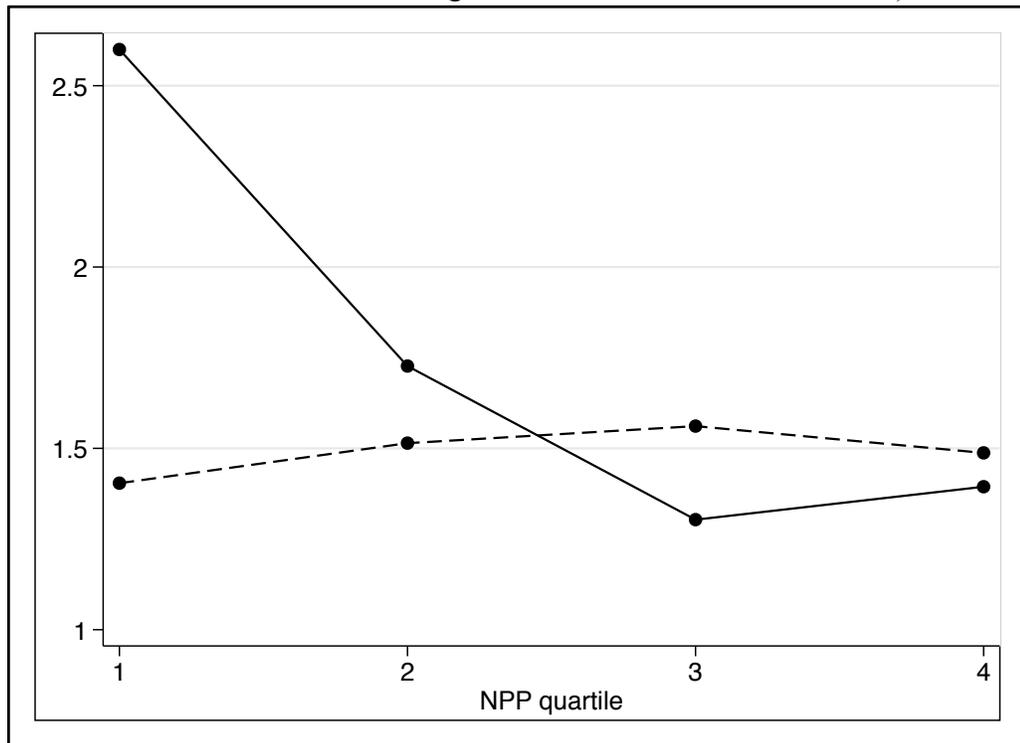


Table 1: Descriptive statistics from the sample of licensing deals, 1995-2014.

	US territory	
	Included	Not included
Number of unique in-licensing firms	913	2,428
Number of deals	2,107	5,117
Percentage of deals	29%	71%
Mean number licensed indications	1.7	1.7
Distribution across development stages*		
Discovery	36%	40%
Clinical trials**	43%	32%
Launched	16%	22%
Unreported	4%	6%
Total	100%	100%

\*Refers to the highest stage of development achieved by the compound at licensing. \*\*Includes deals for compounds undergoing regulatory review.

Table 2: Probability of cooperation by highest achieved stage.\*

Highest achieved stage	Quartile of NPP**				Total
	1	2	3	4	
Panel A: All originator firms					
Phase I	0.23 947	0.25 988	0.29 806	0.3 418	0.26 3,159
Phase II	0.29 1,007	0.3 922	0.36 1,124	0.46 1,071	0.36 4,124
Phase III	0.41 471	0.45 284	0.44 388	0.57 536	0.47 1,679
Launched	0.62 632	0.69 342	0.61 477	0.74 766	0.67 2,217
Panel B: Originator firms without market presence***					
Phase I	0.29 638	0.3 684	0.33 570	0.34 309	0.31 2,201
Phase II	0.33 720	0.33 720	0.41 817	0.52 798	0.4 3,055
Phase III	0.47 307	0.48 205	0.51 266	0.62 387	0.53 1,165
Launched	0.66 140	0.71 98	0.65 133	0.78 200	0.71 571

\*The number of compounds in each cell is presented below the probability of cooperation. \*\*NPP does not include non-specialists. \*\*\*For phase I-III, firms without market presence are the ones without any launched compound. For launched compounds, these are the firms that have produced exactly one launched compound.

Table 3: The value and probability of cooperation. Estimates from linear probability models. The dependent variable equals one if compounds are subject to a cooperation agreement and zero otherwise.

	Panel A: NPP does not include non-specialists			
NPP	0.006**	0.018***	0.017***	0.014***
No Market Presence	0.156***	0.157***	0.181***	0.048**
Constant	0.126***	0.152***	0.261***	0.582***
	Panel B: NPP includes non-specialists			
NPP	0.003***	0.007***	0.009***	0.005***
No Market Presence	0.158***	0.155***	0.189***	0.051**
Constant	0.104***	0.100***	0.170***	0.546***
Highest achieved stage	Phase I	Phase II	Phase III	Launched
N	3159	4124	1679	2217

Legend: \*p<0.1, \*\*p<0.05, \*\*\*p<0.01

Table 4: Percentage of DMMS=1 compounds in the licensing data, by quartile of NPP.

Quartile of NPP	US territory included		Total
	Yes	No	
1 (lowest)	61%	55%	57%
2	84%	84%	84%
3	55%	53%	54%
4	75%	68%	70%

Table 5: Baseline demand, MMS and NPP.

Proxy for downstream demand	MMS	NPP
Total number of patients	-0.09***	0.04
Total number of prescriptions	0.04	-0.07*
Total expenditures on prescription drugs	0.05	-0.11**

Legend: \* p<0.1, \*\* p<0.05, \*\*\* p<0.01

Table 6: Average number of deals by time period.

	US included		US not included	
	DMMS=0	DMMS=1	DMMS=0	DMMS=1
Average number of yearly deals*				
1995-2003 (PERIOD1)	27	59	72	152
2004-2010 (PERIOD2)	39	102	88	199
2011-2014 (PERIOD3)	26	61	93	179
Percentage increases				
1995-2003 vs 2004-2010	44%	73%	22%	31%
1995-2003 vs 2011-2014	-4%	3%	29%	18%

\*Rounded to the nearest integer

Table 7: Estimates from Poisson count models. The dependent variable is the number of deals aggregated at the year/DMMS level.

	(1)	(2)
DMMS	0.80***	0.75***
DMMS*PERIOD2	0.15**	0.06
DMMS*PERIOD3	0.06	-0.10*
Deals include the US		
Sample	Yes	No
Year F.E.	Yes	Yes
N	40	40
Dependent variable		
Mean	53	128
Std. dev.	28	56

Robust standard errors. Legend: \* p<0.1, \*\* p<0.05, \*\*\* p<0.01

Table 8: Estimates from Poisson count models by NPP quartile. The dependent variable is the number of deals aggregated at the year/DMMS level. (Only deals including the US.)

	(1)	(2)	(3)	(4)
DMMS	0.04	1.51***	0.27**	1.18***
DMMS*PERIOD2	0.62***	0.13	-0.18	-0.06
DMMS*PERIOD3	0.48	0.33	0.03	-0.53**
	Quartile of NPP			
Sample	1	2	3	4
Year F.E.	Yes	Yes	Yes	Yes
N	40	40	40	40
	Dependent variable			
Mean	14	17	8	13
Std. dev.	8	14	3	9

Robust standard errors. Legend: \* p<0.1, \*\* p<0.05, \*\*\* p<0.01

Table 9: Short-term licensing response, by stage at licensing. (Deals including the US only.)

	(1) Discovery		(2) Clinical trials		(3) Launched	
	DMMS=0	DMMS=1	DMMS=0	DMMS=1	DMMS=0	DMMS=1
2003	1.0	1.0	1.0	1.0	1.0	1.0
2004	0.7	1.3	1.2	1.9	1.3	1.3
2005	1.6	1.1	0.9	2.0	1.0	1.4
2006	1.3	1.7	0.9	2.3	1.0	1.1
2007	1.6	1.6	1.6	2.4	1.0	0.7
2008	1.9	1.5	0.8	2.3	1.2	1.3
2009	1.1	0.9	1.2	2.2	1.0	0.7
2010	0.8	1.5	1.0	2.0	0.8	1.0

\*For each DMMS/stage category, numbers represent the ratio of total licensing deals observed each year to that observed in 2003.