# International Cooperation in Pharmaceutical Research

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***JEL Codes:*** F13; O34; O57.

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# International Cooperation in Pharmaceutical Research

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December 7, 2011

**Abstract**

This paper aims at examining whether an increased stringency of Intellectual Property Right (IPR) protection is apt to stimulate international cooperation on research projects between developed and emerging countries. To address this issue, we look both at scientific and technological collaborations within the pharmaceutical domain, and we adopt a gravity framework to assess the impact of the IPR level on bilateral R&D cooperation. The analysis is conducted using data from patent and publication databases, and the results provide a sound test of conflicting theories on IPR enforcement and international collaborations in pharmaceutical research.

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# 1 Introduction

In the last decades the need to have a stronger system of Intellectual Property Rights (IPR) has been one of the most debated questions for many countries. On this regard, the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) has represented an important evolution of the IPR regime at the international level. The new rules have been introduced to establish a minimum standard in the protection of the IPR, with the aim to facilitate the transfer of innovation among countries, and to foster the cooperation between the developed and developing world.

It is widely recognized that an effective IPR system may facilitate the transfer of technology in the market for ideas (Nelson and Merges, 1990; Arora *et al.*, 2001; Gans *et al.*, 2002), where organizations prefer to rely on cooperative agreements rather than engage in competition, especially among R&D intensive industries (see D'Aspremont and Jacquemin, 1988; Lerner and Merges, 1998; Hagedoorn, 2002). By cooperating, firms take the advantage to share the cost related to the R&D investments along with a reduction of those investments connected with the commercialization of the invention (Gans *et al.*, 2002). Moreover, R&D collaboration with other sources located in different countries allows firms to engage in joint research programs that offer additional resources targeted to the local needs (Correa, 2007).

To this end, the degree of IPR protection represents a crucial factor in the decision-making about international R&D partnering (Hagerdoorn, *et al.*, 2005). An effective protection of IPR may create incentives to invest in those countries where the development of new invention was based on the imitation process.

Despite the growing theoretical literature about the role played by patents in the innovation process, only scattered empirical evidence is available about the effect of the new IPR system on cooperation and technology transfer at the international level.

In this paper we report a novel empirical strategy to examine whether the increased strength of IPR protection, introduced by the TRIPs agreement, is able to effectively spur the technology transfer measured by international cooperation between selected WTO members. We consider both technological and scientific collaborations focusing on the pharmaceutical industry. The selected industry is the leading example of a science-based sector (Pavitt, 1984), therefore it is important to look at the dynamics characterizing the collaborations both in science and technology. The drug development process heavily relies on the advances in basic understanding of biological processes.

Using a gravity approach, we build a dataset covering a broad international panel of countries over the period from 1978 to 2010, and count the number of patented drugs

and health-related publications jointly signed by researchers located in the developed and developing world. Patents and scientific publications are widely used to proxy, respectively, technological and scientific capabilities of economic agents (Griliches, 1990; Han, 2007).

We use as a natural experiment the new regulations introduced by the TRIPs agreement. Although, the agreement came into force on January 1st, 1995, all developing countries were allowed to retain their own national patent regime until 2000, with special transition rules applied to areas of technology where patent protection was not provided at signing. Pharmaceutical products are the leading example of such a sector, and full protection was required from 1st January 2005.[1] The required changes led by the reform provide an unique opportunity to estimate the impact of a stricter IPR system on technological and scientific cooperation.

Of course the patent system is not the only mechanism available to spur innovation efforts (Chin and Grossman, 1990). Secrecy and licensing agreements can be more effective than patents in the appropriation of the returns from R&D (Cohen *et al.*, 2000; Gallini and Scotchmer, 2001). However, patent protection is particularly relevant in our field of exploration, i.e. the pharmaceutical industry, as this sector does widely rely on patents to appropriate the returns from R&D investments (Cohen *et al.*, 2000; Guellec, 2007).

Our results indicate that the stronger protection of IPR has failed to provide a stimulus to technological pharmaceutical collaborations between the analyzed WTO members, as measured by joint patents. Our finding is in line with the theory that sustains a positive causal relationship between competition and innovation. A reduction in the imitation process due to a stronger patent protection causes a fall in the rate of innovation (see, among others, Aghion *et al.*, 2001, 2005). On the contrary, we find that scientific collaborations benefit from a stronger IPR regime, providing new evidence in the literature discussing the effect of IPR on scientific research (Heller and Eisenberg, 1998; Murray and Stern, 2007; Lach and Schankerman, 2008).

The paper is organized as follows. Section 2 reviews the main literature about international technology transfer and cooperation. Section 3 describes the data and empirical measures used in the analysis, while in Section 4 we test the effect of increased protection of IPR on technological and scientific collaborations and we report our findings. Finally, Section 5 concludes.

[1]The least-developed members of WTO have been recognized the possibility to postpone the enforcement of the new rules to 2016 (see http://www.wto.org/english/tratop_e/trips_e/factsheet_pharm04_e.htm ).

## 2 Literature Review

By means of technology transfer, scholars refer to the wide process by which institution and organizations *interact* with the aim to generate and promote new ideas (see, among others, Bozeman, 2000). No direct measure of international technology transfer exists, and both theory and empirical evidence have relied mainly on material measures, such as foreign direct investments (FDI), trade flows, as well as royalty payments and patents (Gans *et al.*, 2002). Following Bozeman's definition, we compute technology transfer by counting the number of joint patents and publications at the international level. Even though this is admittedly one of the many forms of collaborative research, it has been chosen because it involves direct communication between researchers in the two countries. As a matter of fact, face-to-face situations are essential for ensuring the transfer of both codified and uncodified (tacit) knowledge (Teece, 1981).

The theoretical literature provides grounds to the idea that an increase in the stringency of the IPR can be beneficial for the transfer of technology (e.g. Grossman and Lai, 2004; Valletti and Szymanski, 2005). With an effective IPR system the innovator is more willing to operate where the imitation process is not allowed (Lai, 1998). In a model with endogenous imitation and innovation, a tighter patent law makes more costly the imitation process. As a result, innovators find it advantageous to reallocate their production in those countries where the new IPR system have been introduced (Branstetter and Saggi, 2009). These models follow the Schumpeterian approach according to which the innovation is driven by those firms which become monopolist thanks to the exclusive use of their invention. However from an opposite point of view, if the imitation process is allowed, due to the presence of a neck-to-neck competition, a firm may have incentive to innovate as first (see, among others, Blundell *et al.*, 1999; Aghion *et al.*, 2001, 2005).

Although the theory indicates that the scales are tipped in favor of a positive relationship between IPR and FDI, the empirical evidence is far from being sufficient to confirm this conjecture. It seems that the relationship weakens at higher levels of protection, and the effect is largely dependent upon the characteristics of the country in terms of FDI, import flows, and income level. In particular, in assessing the effects on FDI, we have to consider also that a stronger IPR system causes a reduction in the cost of enforcing licensing contracts, making the use of licensing more attractive, further enhancing the volume of FDI (Yang and Maskus, 2001). Much of this literature underlines how IPR alone is not able to work as incentive to knowledge transfer, also large markets and strong technological capabilities are required (Grossman and Lai, 2004).

Under a different perspective, other studies underline the role of trade in driving

innovation and technology transfer between countries. The basic idea builds on the fact that imports act as a means through which new technologies can be introduced in the receiving countries. Maskus and Penubarti (1995) have used an extended version of the Helpman-Krugman model of monopolistic competition to measure the effect of the patent protection on international trade flows. Their study points out how an increase in the stringency of the IPR can have a positive impact in terms of increased flows of bilateral trade in developing countries. Their results are confirmed by Primo Braga and Fink (1997), who show a positive link between tighter patent protection and manufacturing trade flows. Empirical works analyzing the impact of IPR reforms often do not take into account the efficacy of enforcement, strictly correlated with country's characteristics. Branstetter *et al.* (2006) analyze whether a stronger IPR system accelerates technology transfer. Building on affiliate-level data and aggregate patent data of US multinational firms over the period 1982-1999, they study the effect of patent protection reforms on the royalty payments and R&D expenditures. Their results show that stronger IPR encourages multinational firms to engage in larger technology transfer, as they find a significant rise in the number of patents filed by nonresidents after the IPR reform.[2] More recently, Park and Lippoldt (2008) have studied how trade flows (including licensing and FDI) for different sectors could serve as a means for technology transfer directed toward the developing countries. They investigate the role played by the strength of the new IPR system, as proxied by a set of indicators that includes patents, copyrights and trademark rights. Their results show that trade inflows in developing countries are positively associated with the strength of patent protection, where an enforced IPR system facilitates foreign investments for the development of new innovations.[3] On the contrary, evaluating the effects of TRIPs agreement on new medical treatment, Kyle and McGahan (2011) show that litte R&D efforts have been addressed outside developed countries.

Despite the growing literature about the strategic use of R&D cooperation (e.g. Katsoulacos and Ulph, 1998; Hagedoorn, 2002; Belderbos *et al.*, 2004), little evidence has emerged on its employment under a strengthened IPR system. Firms and institutions may resort to cooperation with the aim to source new ideas for innovations, reducing at the same time the uncertainty associated with these investments. Parallel to this scope, the use of R&D partnerships might be driven by the need to open up new markets or to enlarge market share, and cooperation is likely to happen among rivals (d'Aspremont

[2]However, nothing can be inferred on the welfare effects of a stronger IPR system for these countries, because the analysis does not take into account the impact of the reforms at the national level.

[3]Even though the IPR system encourages firms to invest in R&D devising new technology, the same system discourages them to introduce the second generation products (Scotchmer, 1991).

and Jacquemin, 1988).

International R&D partnerships are very much dependent on the legal system in place in the country partners. A well define IPR system might work as an attraction force for R&D cooperation, especially at an international level where it is expected to be a decisive factor (Coe, Helpman and Hoffmaister, 2009). Exhibiting the characteristic of public good, the introduction of new knowledge may be prevented from a weak patent system especially in those countries where innovation has relied mainly on the imitation process. Instead, with certain appropriability of property rights, joint R&D investments are able to generate positive spillovers, especially among those industries that hinge mainly on patents for the appropriation of R&D returns (Griliches, 1990).

In the Science domain, a growing "anti-commons" argument points to the negative effect of IPR on the free flow of scientific knowledge, by limiting researchers in building on available discoveries (Heller and Eisenberg, 1998). Cooperation within universities and research institutes is generally aimed at different targets, for which the patent system is thought to be irrelevant (Dasgupta and David, 1994). On the contrary, some evidence is provided of a negative impact of IPR protection on the diffusion and utilization of scientific knowledge. Murray and Stern (2007) compare publications whose knowledge is also covered by a patent with publications that are not associated to any patents. By taking into account the dynamics in the citation rate, the authors find that the citation rate of patent-paper pairs (i.e. patent and paper exploiting the same piece of knowledge) declines approximately 10 to 20 percent after the associated patent is granted. However, in a recent analysis Lach and Schankerman (2008) show that research outcomes benefit of pecuniary incentives. Royalty share have some real effects on university research and licensing outcomes, thus suggesting that the IPR regime can positively affect scientific productivity (Lach and Schankerman, 2008).

In this paper we take a dual approach, and we analyze the effect of strengthening IPR both on technological and scientific *collaborations* at the international level in the pharmaceutical domain. We take into account the joint signature of patent documents and scientific articles by researchers located in different countries, providing novel empirical evidence on the role of IPR regime in affecting international cooperation in pharmaceutical R&D.

## 3 Data and measures

Data about the international cooperation in pharmaceutical R&D are drawn and integrated from different sources. Our measure of technological and scientific collaboration

pivots on the information contained in patents and publications. The variables were constructed employing ad hoc queries on *FreePatentsOnline* search engine for inventions (patents) related to pharmaceuticals,[4] and from *ISI Web of Knowledge* for the peer-reviewed research articles published about health-related subjects.[5]

The analysis focuses on collaboration between the developed world and emerging economies. On the one side, we considered North America, i.e. USA and Canada, European countries (including Switzerland due to the presence of the headquarter of top pharmaceutical firms), and Japan. On the other side, emerging pharmaceutical markets are considered, namely Brazil, China, India, Mexico, Russia, South Korea, Turkey. [6]

Based on patents, a measure of technological collaboration between two countries is computed exploiting the information about the country reported in the address of the applicant(s).[7] An international collaboration is counted if a patent is signed by applicants located in two different countries. With this regard, empirical literature has shown that alliances promote technological transfer (Gomes-Casseres *et al.*, 2006); and we use the number of jointly-signed patents as a proxy for successful alliances (Kim and Song, 2007). In order to identify pharmaceutical patents, the classes A61K and A61P of the International Patent Classification (IPC) are considered.[8] The patents granted over the period 1978-2010 have been extracted from the database.

Information about health-related research articles published over the same time period are drawn from *ISI Web of Knowledge*.[9] The database reports the affiliation of all the authors involved in a publication, along with their full address. A scientific col-

[4]The *FreePatentsOnline* search service enables full-text search of published international patent applications from 1978 (see http://www.freepatentsonline.com). The analysis of international collaboration is based on the count of patents submitted to the World Intellectual Property Organization (WIPO), i.e. patents under the Paris Convention Treaty (PCT) are considered. These patents have been preferred to patents applied for at national offices (e.g. NBER patent database comprising patents granted by the US patent and trademark office, or patents at the European patent office), as we expect patents jointly applied for by developed and emerging countries to be intended to protect innovations both in the developed and emerging countries, and WIPO-PCT is intended to get such a wide coverage.

[5]See http://apps.isiknowledge.com.

[6]The selected countries were originally identified by a leading consultant firm in the health care industry as the emerging pharmaceutical markets (IMS Health; see http://www.imshealth.com). These countries are included among the developing countries by the World Bank with the exception of South Korea (among high-income countries from 1997).

[7]The applicant (or assignee) is the organization who first claims to be the inventor and holds full rights to the innovation.

[8]The class A61K includes "preparations for medical, dental, or toilet purposes", whereas the class A61P considers the "therapeutic activity of chemical compounds or medicinal preparations". For further details see: http://www.wipo.int/classifications/ipc/ipc8/?lang=en.

[9]Since journals publish scholarly material in a variety of matters, we confine our data to research articles that are defined by their health-related contents. Particularly, the database was queried for articles containing the following terms: pharma OR biotech OR drug OR therapeutic OR disease OR medical.

laboration between two countries is considered if the publication is jointly signed by researchers located in both countries (Glänzel and Schubert, 2005).

Besides the number of collaborations, *FreePatentsOnline* and *ISI Web of Knowledge* are also employed to measure the total production of each countries, respectively in terms of pharmaceutical patents and scientific publications (Griliches, 1990; Han, 2007).

Two measures of the level of IPR protection are considered. We rely on data provided by the *World Economic Forum* (WEF) and also published by the *Economic Freedom Network* (EFN, see Gwartney and Lawson, 2008), henceforth referred to as PIPR (protection of IPR) index,[10] as well as on the index of IPR protection developed by Park and colleagues (Ginarte and Park, 1997; updated in Park, 2008). The latter measures the strength of patent protection by aggregating five separate scores on coverage, international treaties, duration of protection, enforcement mechanisms, and restrictions (Park, 2008). On the contrary, the index developed by the WEF is based on a survey capturing the opinion of business executives about IPR protection. It comprises information not only based on the subject matter that can be patented, but also about the length of protection, the mechanisms for enforcing patent rights, the evolution of the international patent laws (Park and Wang, 2002). The index measures the strength of the legal structure and security of IPR.

Average values of the Park index for the countries included in the study is presented in Table 1, whereas the evolution of the PIPR index is reported in Figure 1.

The Park index shows an increase in the protection of IPR by emerging economies (from 2.570 in 1995, to 3.904 in 2005), even though the index is still lower than the corresponding value for developed countries (3.904 versus 4.555 in the latest avaiable time period). The PIPR index shows a slight increase in the year 2005 for the emerging markets, but in the year 2009 figures are back to pre-2005 values. The general perception about the effect of TRIPs on IPR protection decreases few years after its full adoption in the emerging markets.

[10]The Global Competitiveness Report relies on the Executive Opinion Survey, by which participants evaluate on scale of 1 (the lowest) to 7 (the highest), the current conditions of their operating environment. The Survey is carried out among (mainly large) firms representing the main sectors of the economy, asking questions about different aspects of the economy (including, e.g. institutions, infrastructures, higher education and training, etc.). As for our analysis, executives are asked to provide a rate to intellectual property protection (including anti-counterfeiting measures) in their own country, with 1 corresponding to very weak protection and 7 to very strong protection. This index is the source of the data published by the EFN (Gwartney *et al.*, 2008), that is tranformed on a 0-10 scale. We used data from both sources keeping the 0-10 scale measure (For complete methodological details see www.weforum.org and www.fraserinstitute.org). More specifically, the EFN reported the index of protection of IPR before the year 2005 and then switched to the more general index of protection of property rights. For the years 2005-2009, we accessed the data by the WEF for the index of protection of IPR (transforming the index from the 1-7 to the 0-10 scale).

| Park index | | 1995 | 2000 | 2005 |
|---|---|---|---|---|
| Emerging markets | Mean | 2.570 | 3.493 | 3.904 |
| Developed countries | Mean | 4.273 | 4.506 | 4.555 |

Table 1: Average value of Park index for the emerging markets in our study (Source: our computations on Park, 2008).

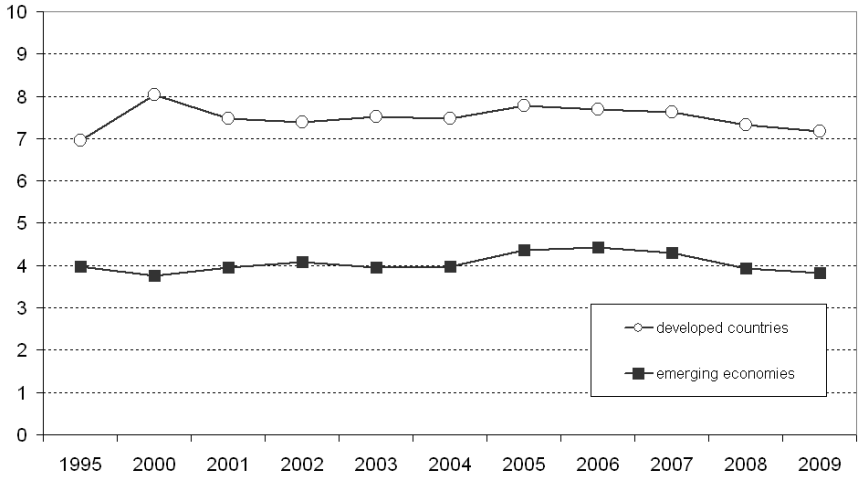


Figure 1: Average value of the index of protection of IPR, 1995, 2000-2009 (Source: our computations on WEF and EFN data)

# 4 Methodology and results

Gravity models have been successfully employed for studying the determinants of bilateral flows (Anderson and van Wincoop, 2003). Building on the Newton's law of universal gravitation, the model posits that the flow $F_{ij}$ between two countries $i$ and $j$ is proportional to their "masses" (respectively $M_i$ and $M_j$) and inversely proportional to the distance between them $D_{ij}$:

$$F_{ij} = \frac{\beta_0 M_i^{\beta_1} M_j^{\beta_2}}{D_{ij}^{\beta_3}} \tag{1}$$

The gravity equation has been most commonly applied to study trade flows, but it has also been employed to study migration flows, equity flows, FDI, and knowledge flows (see e.g. Portes and Ray, 1998; Peri, 2005). Previous literature has also considered a gravity framework for studying the internationalization of R&D activities looking at joint patents by inventors/applicants from different countries (Picci, 2010).

The empirical literature has taken into consideration various forces on the right hand size, such the effect of common language or international treaties (see e.g. Anderson and Van Wincoop, 2003). We investigate whether there is a role for more stringent IPR in fostering technological and scientific collaborations between developing and developed world. Particularly, we aim at understanding whether the increased stringency in IPR in the emerging markets has resulted in an increased collaboration with the developed world.

In order to obtain an estimate of the parameters in equation (1), the model is customarily log-linearized and ordinary least squares is applied. This traditional approach has been recently subject to a strong critique, as it fails to provide a consistent estimate of model elasticities if heteroschedasticity is present in the original equation (Santos Silva and Tenreyro, 2006). As a robust alternative, the Poisson pseudo-maximum likelihood estimator is to be preferred, allowing the researchers to solve the consistency issue, as well as the possibility of zero flow between two countries.

In our analysis, the empirical assessment of the technological and scientific collaboration relies, respectively, on the number of patents co-applied by agents located in countries $i$ and $j$, and on the number of joint publications by scientists located in countries $i$ and $j$.

Let $C_{ijt}$ be the measure of technological and scientific collaboration between country $i$ and country $j$ at time $t$. Collaboration between North American and European countries ($i$) and selected emerging markets ($j$) is taken into account. A gravity equation is considered, where we include the IPR regime of country $j$ ($PIPR_{jt}$; $ParkI_{jt}$, generally

referred to as $IPR_{jt}$) among the attraction forces:

$$E[C_{ijt}|X_{ijt}] = \exp(\beta_0 + \beta_1 \log M_{it-1} + \beta_2 \log M_{jt-1} + \beta_3 \log IPR_{jt} + \tau_t + \alpha_{ij}), \quad (2)$$

with $\alpha_{ij}$ representing a dyad-specific characteristics that are invariant over time (including geographical distance), $M_{it-1}$ and $M_{jt-1}$ the "masses" of, respectively, country $i$ and $j$,[11] and $IPR_{jt}$ measures the level of enforcement of IPR, proxied using both the index of IPR protection published by WEF/EFN (PIPR) and the Park index (Park, 2008). Time dummies are included in all specifications ($\tau_t$).[12]

In order to proxy $M$, the international trade literature has relied on GDP and population measures. Following the Schumpterian tradition, here we make use of the patent stock per country when analyzing the technological collaborations, and the publication stock in the case of scientific collaborations in order to measure technological and scientific capabilities at the country level within the pharmaceutical domain (Han, 2007).[13] The stocks are defined as

$$G_{k,t} = P_{k,t} + (1 - \delta)G_{k,t-1}, \quad (3)$$

with $k$ representing the country index and $t$ is measured yearly from 1978 to 2010.[14] We rely on the industry-specific estimate of the depreciation rate provided by Park and Park (2006). We apply the value for the chemical sector (also comprising pharmaceuticals) considering $\delta = 13.11\%$.[15]

The model is estimated using the pre-sample mean estimator (PME) proposed by Blundell *et al.* (1995; 2002) that allows for correlated fixed effects $\alpha_{ij}$ and predetermined variables (see also Windmeijer, 2008).[16] The estimator allows us to explicitly tackle the possibility for correlation between the regressors included in the model and the dyad-

[11] One-year lag is considered in order to avoid endogeneity, as masses at time $t$ also include cooperation at time $t$.

[12] Over the analyzed time period, the Park index is only available for two years: 2000 and 2005. Therefore the number of available observations is drastically reduced. In order to solve this issue, we follow Picci (2010) and "extend" the Park index, imputing the value for the year 2000 to the years 2001 and 2002, and the value for the year 2005 to the year 2003-2007.

[13] In (unreported) preliminary analysis we experimented with various measures including GDP, R&D expenditure, the number of researchers, and pharmaceutical production. The results were largely unsatisfactory as the coefficients associated to these measures were largely insignificant posing concerns about the ability of selected proxies to act as a measure of the "mass" of the countries.

[14] As the number of international patent applications were negligible before the year 1990, in the case of patent, the knowledge stock is computed considering data from 1990.

[15] Pharmaceuticals and chemicals patents are characterized by slow rates of depreciation (Schankerman, 1998). Different studies show that the pharmaceutical R&D (both basic research and applied research and development) use a declining balance formula with a depreciation rate no greater than 15% (Hall *et al.*, 2005).

[16] Estimates are performed using Stata 11.

specific component $\alpha_{ij}$.[17] The pre-sample mean estimator is preferred to a fixed effect Poisson estimator as it also allows for the presence of feedback effects between the variables on the right hand side and the error term. We expect a dynamic effect to be at work in this context, where collaborations at time $t$ could produce beneficial effects for both countries at time $t+1$ and enhance the production of knowledge. Standard errors are estimated using the methodology proposed by Cameron *et al.* (2006) that allows cluster-robust inference in the case of non-nested two-way clustering.[18]

As in the case of technological collaboration, our data record a large incidence of zeroes (about 75% of observations record no jointly signed patent), we also take into account the decision to enroll in a collaboration where the dependent variable identifies a binary outcome: $\tilde{C}_{ijt} = 1$ if at least one joint patent/publication is recorded between country $i$ and country $j$ at time $t$ , i.e. $\tilde{C}_{ijt} = 1$ if $C_{ijt} > 0$. A random effect probit model is considered.[19]

Application of the pre-sample estimator is allowed by the availability of information on the dependent variable before the year 2000 (corresponding to the first year from which data about IPR protection as measured by PIPR are continuously available). Particularly, we collected information about joint cooperation in patents and scientific publications from the year 1978.[20] Descriptive statistics of the variables included in the regressions are reported in Table 2.

Figure 2 depicts the dynamics of the average value of our dependent variables. The year 2004 (right before the deadline for TRIPs enforcement) seems to be a break-point in the dynamics characterizing collaboration in patents, whereas this is not the case for scientific publications. Need it here to stress the fact that patents are recorded according to the application date, that is closer to the actual timing of the patented invention than the publication date. This explains the lower value of collaborations in patents recorded in 2010.[21]

[17] As a result, we are not able to estimate the effect of the distance between the two countries (as time-invariant, and therefore included in $\alpha_{ij}$). However, this effect is not directly of interest to our research.

[18] In our context, it is not possible to assume independence among the dyads. As an example, dyad $ij$ is correlated with dyad $ik$ even if $j \neq k$, due to the presence of county $i$ in both dyads.

[19] In the case of scientific publications, only 3% of the observations record no collaboration, therefore the analysis only relies on count data models.

[20] However, in the case of patents, due to the limited number of PCT application before the year 1998, only the years 1998 and 1999 are used to compute pre-sample averages.

[21] Put it differently, patent data for the year 2010 are censored, due to the time lag between the application date and the publication date (on average 1 year when PCT-WIPO patents are considered, based on our computations). The data for the year 2009 and 2010 will not be used in the regressions analyzing collaboration in patents. On the contrary, all available observations are exploited in the estimation of the publication equation. Still, data about $PIPR$ are available over the period 2000-2009.

| Variable | Mean | Std. error | Min | Max |
|---|---|---|---|---|
| **Patents** | | | | |
| pt_coop | 3.886 | 15.74 | 0 | 152 |
| $M_i$ (patent) | 3780 | 7647 | 5.035 | 47444 |
| $M_j$ (patent) | 702.6 | 957.6 | 4.248 | 8634 |
| **Publication** | | | | |
| pu_coop | 58.48 | 145.6 | 0 | 2561 |
| $M_i$ (publication) | 51891 | 80845 | 1194 | 457312 |
| $M_j$ (publication) | 13054 | 12163 | 3117 | 156464 |
| **Protection of IPR** | | | | |
| PIPR | 4.056 | 1.089 | 1.900 | 7.300 |
| Park index | 3.699 | .4936 | 2.270 | 4.330 |

Table 2: Descriptive statistics

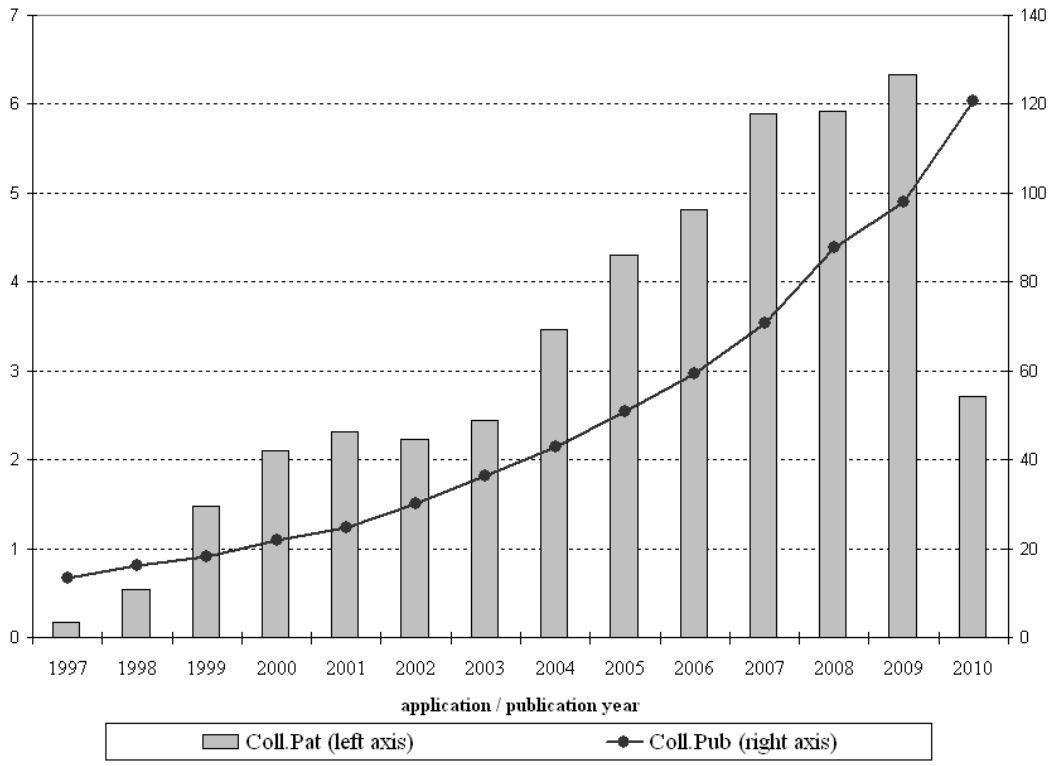


Figure 2: International R&D collaboration in patents (bar, left axis) and publications (line, right axis), sample average

Table 3 reports the estimation of the model of technological collaboration as in equation (2), taking into account the number of, respectively, patents and publications jointly located in country $i$ and $j$.

The country masses $M_i$ and $M_j$ (as measured by knowledge stock), all have the expected sign and are statistically significant. The larger the knowledge base of each country involved in the collaboration, the higher its "attraction force".

With regards to the stringency of IPR, a different effect of the new rules introduced by the TRIPs agreements on technology and science is highlighted by the regressions.

The index of IPR protection exerts a negative effect on research cooperation gauged by patents in pharmaceuticals. Stronger protection of IPR fails to provide a spur to technological collaboration between countries, as measured by the joint ownership of the rights to innovation (trough patents) in pharmaceuticals. One possible explanation is that these results represent a premature investigation on the effects of the stringency of IPR in those countries for which the patent protection belongs to the recent history. However, these results confirm the theoretical prediction of some studies for which increased national patent protection cuts competition, diminishing the incentives for more investment in R&D (Helpman, 1993; Aghion *et al.*, 2005).

Within the pharmaceutical domain, although the increased strength of IPR protection has not risen technological collaborations, we find a positive influence on the number of joint publications. The opposite sign of our results on technological and scientific collaborations could be explained considering the dual nature of scientific knowledge. In the long term R&D investments, in particular, the distinction between basic and applied research tends to vanish. Following the "Pasteur's Quadrant" terminology (e.g. Stokes, 1997), joint research projects are carried out with the complementary goals of creating a product having a commercial value (patents), and broadening the scientific knowledge (publications) (Gans *et al.*, 2011). What our results seem to suggest is that the use of the patent in pharmaceuticals is likely to be postponed to later stages in order to favor further efforts in the research process starting from the initial idea (Heller and Eisenberg, 1998). In particular, this is true when scientists are independent to address their research following their own interests (Aghion *et al.*, 2008). The "anti-commons" literature points exactly to the proliferation of patents as the cause of resources underutilization, since the presence of numerous patent owners obstacles future cooperation in research (among others see Heller and Eisenberg, 1998). The likelihood of this contention, of course, needs to be verified in the future using a longer time span. Moreover, the decline in joint patents following the IPR reform might be explained considering

On the contrary, all available time periods are used in the analysis of joint publications.

| | Patents | | | | | | Publications | | |
|---|---|---|---|---|---|---|---|---|---|
| | Probit RE | Probit RE | Probit RE | Count PME | Count PME | Count PME | Count PME | Count PME | Count PME |
| IPRR measure | PIPR | Park | Park$^{(a)}$ | PIPR | Park | Park$^{(a)}$ | PIPR | Park | Park$^{(a)}$ |
| $M_{it-1}$ | .7123*** | .6965*** | .7357*** | .6386*** | .7459*** | .6975*** | .3218*** | .2685*** | .2927*** |
| | (.0435) | (.0881) | (.0625) | (.0753) | (.0300) | (.0041) | (.0383) | (.0547) | (.0514) |
| $M_{jt-1}$ | .5397*** | .6625*** | .4315*** | .6847*** | .7753*** | .6700*** | .6531*** | .6405*** | .6552*** |
| | (.0804) | (.0906) | (.0391) | (.0886) | (.1395) | (.0799) | (.1759) | (.2152) | (.1865) |
| $IPRR_{jt}$ | -.9881** | -2.675*** | -.8803*** | -.3634 | -3.689*** | -1.020*** | .3432** | 1.157*** | .3901*** |
| | (.4867) | (.8491) | (.3116) | (.5844) | (.4246) | (.1381) | (.1586) | (.3467) | (.0837) |
| Pre-sample | | | | .9760*** | .9362*** | .9238*** | .7992*** | .8769*** | .8427*** |
| | | | | (.0639) | (.0670) | (.0498) | (.0813) | (.0653) | (.0753) |
| Constant | -6.022*** | -4.478*** | -3.985*** | -7.139*** | -5.166*** | -5.027*** | -7.538*** | -8.005*** | -8.242*** |
| | (.4364) | (.9994) | (.7758) | (1.030) | (.1929) | (.6508) | (1.542) | (2.258) | (1.865) |
| Obs. | 1071 | 238 | 952 | 1071 | 238 | 952 | 1190 | 238 | 952 |
| Log-lik. | -403.86 | -80.97 | -343.76 | – | – | – | – | – | – |

Time dummies included in all specifications.
Statistical significance: *** 1%, ** 5%, * 10%.
Standard errors robust to multi-way clustering in parenthesis (Cameron *et al.*, 2006).
$^{(a)}$ Value of the Park Index for the year $t$ is used for the period $(t-2, t+2)$ (Picci, 2010).

Table 3: Gravity model of research cooperation, patents and scientific publications

that a better defined system of rules about IPR presumably favors scientific cooperation among scientists in developed and emerging countries, making unnecessary the recourse to the patent to protect an idea at the early stage of the research process.

# 5 Concluding remarks

In this paper we answered the question whether the dynamics of the international cooperation in pharmaceutical research changes in response to an increased stringency of the IPR protection. This research has been motivated by the recent trends in the protection of the IPR system at the global level. Little evidence is available about this issue and we contributed to the literature by exploring the effect of IPR on the research cooperation at the international level.

Cooperation in R&D is a key factor in the pace of innovation if we consider that the disclosure of new ideas depends on a complex and interacting set of institutions, and the joint ownership in R&D investment is a widely used strategy.

We estimated a gravity framework on the number of joint patents and scientific publications, focusing on the pharmaceutical research cooperation between developed and developing countries. We obtained evidence of a negative effect of the stringency of the IPR protection on the level of technological collaboration (joint patents), whereas positive influence seems to be exerted on scientific collaboration (joint publications). This opposing results might be explained referring to the recent "anti-commons" literature where the use of patents at the early stage of the research process curbs the competition, slowing down the rate of innovation. On the other hand, a decline in joint patents could be explained by arguing that a more reliable system of IPR makes patents no more necessary to be applied at the very beginning of the innovation process.

Two limits of our work have to be acknowledged. First, we examined the research efforts between countries, but not tackle the issue of the effectiveness of a stricter IPR system in promoting technological innovation at the country level, along with an assessment in terms of economic growth. Second, our definition of collaboration relies on jointly signed patents and papers, which is admittedly a narrow form of collaboration, but nonetheless entailing the transfer of both codified and uncodified knowledge.

Finally, since the reform of the IPR system is very recent, interesting would be in future to consider a longer time span, along with a wider set of industries, in order to let the countries develop the institutions and capabilities apt at fostering collaboration between the developed and the developing world.

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