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# Big Pharma and monopoly capitalism: A long-term view

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ABSTRACT

Are intellectual property rights institutions meant to foster innovative activity or conversely to secure appropriation and profitability? Taking stock of a long-term empirical evidence on the pharmaceutical sector in the US, we can hardly support IPRs intended as an innovation rewarding institution. According to our analysis, pharma patents have constituted legal barriers to protect intellectual monopolies rather than an incentive and a reward to innovative efforts. Patenting strategies appear to be quite aggressive in extending knowledge borders and enlarging the space protected from the possibility of infringement. This is also witnessed by the fact that patent applications are very skewed in the covered trade names and patent thickness expands over time. Conversely, the ratio of patents protecting new drugs approved by the FDA which draw upon government-sponsored research – as such, a mark for quality – falls. Firm-level analysis on profitability confirms strong correlation, restricted to publicly traded pharmaceutical companies, between patent portfolio and profit margins.

## Introduction

The role of patents has been the subject of extensive research, debate, and heated controversy for a long time. As early as 1950, Fritz Machlup and Edith Penrose gave a very lucid account of such controversy and concluded that no decisive arguments exist either in favor or against patents (Machlup and Penrose, 1950). A few years later, Machlup himself wrote a detailed report for the Subcommittee on Patents, Trademarks, and Copyrights of the United States Senate and expressed the same doubts: "*none of the empirical evidence at our disposal and none of the theoretical arguments presented either confirms or confutes the belief that the patent system has promoted the progress of the technical arts and the productivity of the economy*" (Machlup, 1958, p. 79).

The basic argument is well known. Potential innovators do not have incentives to invest in the production of new technological knowledge if they cannot appropriate the returns of innovation, since knowledge tends to diffuse and is easily imitated by competitors. Such appropriation of returns can only be ensured by departing from purely competitive conditions and granting the innovator some legally protected monopoly power. Pushing this argument to its extreme consequences, one could argue that society faces a dilemma between incurring the social costs of monopoly, for which the innovation will be available at higher prices and lower quantities than in perfect competition, or incurring the social cost of not having the innovation at all because innovators refrain from investing in R&D.

This argument has been criticised on many grounds. First, several empirical studies have questioned the assumption that, without patent protection, innovative knowledge is easily imitated by competitors. Levin et al. (1987), for instance, reports that patents are usually considered less important than learning curves and lead times to protect product innovation, and even less effective when process innovations are concerned. Building on this, the so-called 1994 Carnegie Mellon survey (Cohen et al., 2000) presents a detailed study on the incentives to undertake R&D and reports that, as far as product innovations are concerned, the most effective mechanisms are secrecy and lead time, while patents are the least effective, with the partial exception of drugs and medical equipment. Nevertheless, the role of patents has increased in the last decades, showing that perhaps they are used for other purposes than appropriating the returns from innovation (Hall et al., 2005). More recently, Arora and Ceccagnoli (2006) use the Carnegie Mellon survey to study the relationship between propensity to patent and propensity to license, and find a positive correlation only for those firms which lack complementary assets while, for firms that do possess such complementary assets, the correlation is negative. Branstetter et al. (2006) study how changes in patent regimes influence technology transfer and find that the effects are mostly confined within affiliates of

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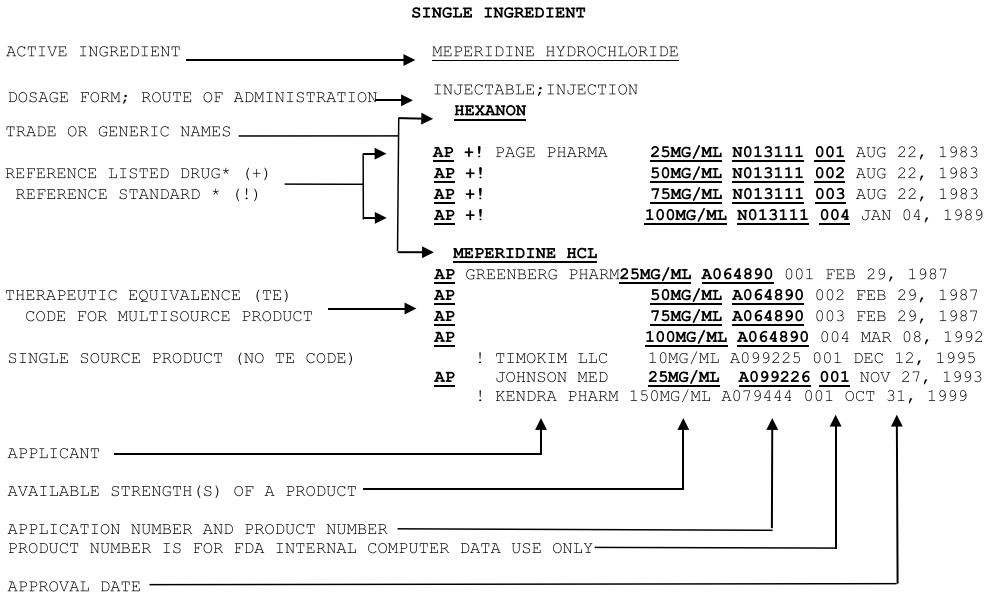



**Fig. 1.** Drug product illustration. Source: Orange Book (2021).

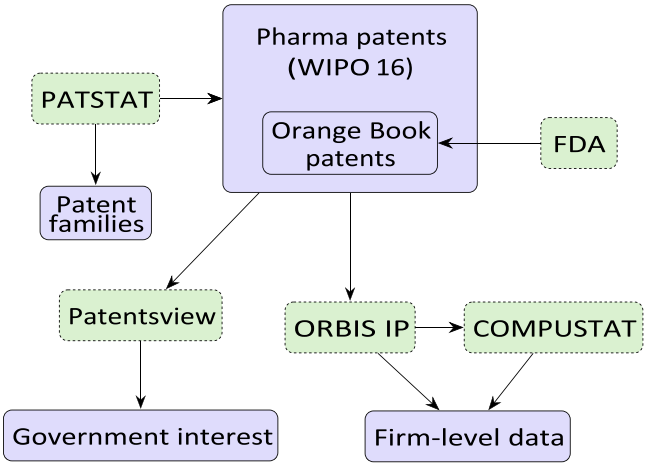



**Fig. 2.** Flowchart of the empirical analysis.

parent companies.

Another issue concerns, first, the extent of such departure from competitive conditions, that is the actual or expected extra-profit necessary to trigger innovative search and, second, the possible monotonicity in the relationship between such departure and the intensity of innovative effort. These questions are particularly thorny with respect to the scope and breadth of patents. In one perspective, which we may call the *incentive view*, patents, by restricting the possibility of imitation, grant the innovator a monopoly rent which should motivate *ex-ante,* and compensate *ex-post,* the R&D investment. In the alternative perspective, which we may call the *opportunity view*, innovative activity is primarily driven by the richness of opportunities of technological advances, while patents represent intellectual barriers to innovation and obstacles to its diffusion. Whether being institutional forms embraced to secure rents or to ensure legitimate profits, both streams recognise patents as creators of intellectual monopolies, even if in the former case they are a necessary evil to drive the "unbound Prometheus" of innovation in capitalist societies, while in the latter case they primarily act as a generation mechanism of unproductive rents (Dosi et al., 2006).

Among all sectors, the pharma has been recognised as one of the most dependent on patents in order to ensure its intellectual monopoly. The reliance of pharma on patents – it is commonly claimed – descends from the very nature of its production activity, based on very low reproduction costs, and facing instead almost exclusively entry costs in terms of knowledge generation. Given the potentially easy replication of the knowledge embedded in a product (Dosi and Nelson, 2010), patents ensure a temporary exclusive use of such knowledge, which would otherwise be simply acquired by competitors. Additionally, the knowledge embedded into pharmaceutical patents is often discrete and naturally apt to be confined into patent claims (Orsenigo and Sterzi, 2010).

Our evidence challenges the correspondence between patents and innovation, and studies the behaviour of modern monopoly capitalism ensured by intellectual rents in the long run, adopting a historical perspective to detect the change in the IPRs system within the pharma industry (Khan and Sokoloff, 2001) and the current evolution of capitalism directed toward an accelerated *commodification of knowledge* (Coriat and Weinstein, 2012), or equivalently toward *rentification* (Dosi and Virgillito, 2019). The historical analysis allows to frame the evolution of patenting activity in the pharma industry also comparatively, to appreciate the *diversity of modern capitalism*, in the words of Amable (2003).

Let us start by noticing that historical records (see for instance the monumental account by Sneader, (2005)) show that, until very recently, drug discovery has been mainly driven by search heuristics that lie very far from mere appropriation objectives, even when undertaken within corporate laboratories. More specifically, the modern pharmaceutical industry was born – mainly in Germany – under a regime of basically non-existent patent protection and then, after 1877, thrived under a regime of rather weak protection of processes, rather than products. Still, the chemical/pharmaceutical oligopolies – later merged in 1925 into one monopolist firm, IG Farben[1] – were able to reap hefty profits stemming from the integration of "pure" scientific research, in close collaboration with universities, applied product-oriented research, industrialisation and scaling-up of production, market penetration, and

[1] IG Farben, a short common name for Interessengemeinschaft Farbenindustrie AG, was formed in 1925 as the merger of the six main chemical/pharmaceutical German companies: BASF, Bayer, Hoechst, Agfa, Chemische Fabrik Griesheim-Elektron, and Weiler-Ter Meer. The company survived until 1951, when it was split in its originally constituent companies (Beer, 1959).

product diversification. At the turn of the 20th century, the leading German dyestuff companies were paying annual dividends between 18 and 26% (Plumpe, 1991).[2]

The German chemical/pharmaceutical industry is the first to enter the era of modern monopoly capitalism. We use this term as a shorthand for industrial regimes characterised by a) either few oligopolistic firms, or indeed a monopoly like the one of IG Farben in 1920s and 1930s Germany, or of platform firms nowadays; and b) their ability to secure a sustained stream of differential profits/rents. Monopoly capitalism may be either due to complementary assets (Teece, 1986) and distinct organisational capabilities (like the aforementioned, with reference to the 19th century German chemical industry), or due to the consequences of extreme increasing returns in information-intensive activities (such as those associated with contemporary platform technologies), or due to the sheer outcome of monopolistic rights over crucial tangible or intangible assets, such as patents.[3]

The very history of the pharmaceutical industry highlights that there is no necessary link between profits/rents accruing to monopoly capitalists, as defined here, and rates of innovation, and even less so between the latter and the appropriation of knowledge via patents. The modern drug industry emerges basically out of dyestuff and the development of synthetic chemistry for new compounds (Beer, 1959). In the early days, the "incorporation of science" and the "industrialisation of invention" involve close connections between university and industry, between research and production, and the cooperation of chemists, engineers, and technicians (Marsch, 1994). In this, German-centered, institutional set-up, IPRs in the form of patents play no role at the start, and become important in the early 20th century only as a defensive weapon against foreign imitation. All this notwithstanding, or because of this, the rates of innovation have remained very high.

The US drug industry in the first 80 years or so plays a negligible role, also because, unlike Germany, it is largely separated from the chemical industry. Things change dramatically with World War II, and the mass production of penicillin is the archetype of such a change. Penicillin was discovered in the UK, but industrialisation and scaling-up of production occurred in the US, under the guidance of the Federal Office of Scientific Research and Development, founded by the Federal Government, which retained all IPRs while freely sponsoring private production under non-exclusive conditions (Best and Bradley, 2020; Gross and Sampat, 2020). That was basically the template upon which the US drug industry surged to world leadership, with non-profit institutions (public laboratories and universities) undertaking a most of the basic research and also product development.[4] Under that institutional arrangement, private pharmaceutical companies were receiving publicly generated knowledge basically for free, but they were engaged into a good deal of basic research too, even if with the only purpose of efficiently absorbing, refining, and industrialising it. Thus, when private appropriation was possible (it could not be done on the results of publicly financed research), it occurred quite "down the line" and still had very little to do with any incentive to search for innovative knowledge.

This picture started to change under the convergence of different factors. The Bayh Dole Act of 1980 allowed patenting of the outcomes of publicly sponsored research. The jurisprudence increasingly enlarged the domain of patentability, while at the same time becoming much less demanding on the criterion of novelty. No refinement of comparability has even been put in place: that is, patent applicants have to show that a certain drug somehow works, but not that it works better than already existing ones (so-called prior art, in patents jargon).[5] Additionally, since the 1990s, a good deal of running costs of the US Food and Drug Administration, namely the regulator, have been put in charge of drug companies, i.e. the regulated actors.

All in all, since the mid 1970s but more rapidly since the 1980s, patenting has exponentially increased, with no evidence, however, of any parallel increase in the rates of innovation. On the contrary, the pharmaceutical sector has been recently object of policy and scientific concerns of an *innovation crisis*. Indeed, according to Light and Lexchin (2012) there is a myth of such a crisis in pharma, but there is also a real innovation crisis of a different nature. The myth stands in the purported decline in the number of released New Molecular Entities (NMEs) which, however, after the resolution of a backlog in applications, settled at an average between 15 and 25 drugs per year, with one NME per firm approved every six years, on average, and most successful companies recording one NME per year, and with a constant production rate in the last fifty years (Munos, 2009). The real innovation crisis comes from the lack of new therapeutical treatments in new drugs which, since the 1980s, have been introduced at disappointingly low rates. Different studies agree that the innovativeness of therapeutic treatments has been quite low, with reference to new drugs approved in the EU (Motola et al., 2006; Van Luijn, Gribnau, and Leufkens 2010), Canada (Morgan et al., 2005), and the US (Angell, 2005).

The different phases of the patent regimes in the US described so far closely mimic the timeline proposed in Coriat and Weinstein (2012) describing a *Pre-Fordist* phase, marked by the intention to reward the individual innovative activities and during which firms tend to acquire knowledge from outside, until the establishment of *Corporate Capitalism* in which innovation laboratories were created inside vertically integrated and hierarchical firms, mainly big ones, while structured relationships with universities and public laboratories emerged. The third phase, initiated by the Bayh-Dole Act of 1980 (Coriat and Orsi, 2002), defines instead an acceleration in the commodification of knowledge and paves the way for the rentification of innovative activities and the innovation crisis in pharma.

In the latest phase, most new approvals appear to reflect defensive patenting around existing compounds and therapies, new applications of existing molecules, and so-called "*me-too*" drugs. While it is not easy to clearly identify "*me-too*" drugs, Krieger et al. (2018) provide compelling empirical evidence of their increase. They calculate an index of similarity between drugs by computing a Jaccard distance between chemical substructures. They then apply this measure to data in Thomson Reuters Cortellis's Investigational Drugs database, which contains detailed development histories of over 64,067 drugs, and find that the number of molecules presenting a similarity score of 0.9 or above has more than doubled in the period 1999–2014.

Also the expenditure of large pharmaceutical companies in basic R&D has been dramatically low (Light and Lexchin, 2005), in line with a general reduction in the involvement of private corporations in science (Arora et al., 2018). Public funding on the contrary has become more and more important for relevant discoveries (Li et al., 2017; Lichtenberg and Sampat, 2011). For instance, Cleary et al. (2018) report that the NIH

[2] Another interesting case is that of the Swiss pharma industry, developed mainly around the city of Basel, near the German border, under a regime of heavy imitation of German capabilities (Tanner, 1998) and then switched to a different regime of strong patent protection and enforcement only in 1970s, after reaching world leadership.

[3] See Lazonick (1992) for an extensive critical discussion of the role of technology, organisation and competition in capitalistic development, and Pagano (2014) for a focus on the role of intellectual property rights in monopoly capitalism.

[4] Moser, Voena, and Waldinger (2014) argue that also the migration of Jewish scientists from nazi Germany played a major role in boosting US innovative performamce.

[5] In fact, the regulatory framework has been even worse, neglecting basic safety requirements for a long time. Just as an example, in 1937 the company Massengil commercialised a poisonous antibiotic (Elixir Sulfanilamide) which caused the death of more than 100 people; Massengill could be prosecuted only for mislabelling. Even the Kefauver Harris amendment, approved in 1962 after the thalidomide tragedy, failed to provide general third-party check requirements for safety (Temin, 1985, Angell, 2005, Avorn, 2005).

funding contributed to published research associated with 210 NMEs approved in the period 2010–2016.

Coupling together the two latter trends, namely the innovation crisis and the decrease of breakthrough innovations produced by private companies, this paper provides a systematic analysis of the patenting activity in the pharmaceutical sector, distinguishing between product and process innovations. By reconstructing the long-term evolution of all drugs approved in the Orange Book by the Food and Drug Administration, we disentangle the increasing role of public funding in process-based innovation (overall pharmaceutical patents) and the decreasing one in product-based innovations (Orange Book). After studying the evolution of standard quality indicators, we focus on a rarely used indicator of appropriability, namely extended patent families, and document the changing patterns over time of top collecting families and relative firm applicants.

Finally, leveraging on Compustat, we look at the dynamics of sales, profitability, and R&D activity of top patenting listed firms. Our analysis reveals that inside a vast variety of firm-level strategic patenting behaviours, patent porfolios strongly correlate with profitability, and only to a lesser extent to R&D expenses.

The rest of the paper is organised as follows. Section 2 presents the data and methods that have been used. Section 3 provides evidence of the so-called innovation crisis in the pharmaceutical sector, while Section 4 explores the firm-level relationship between appropriability, profitability and R&D expenses. Finally, Section 5 concludes.

## Data and methods

We base our analysis on patents belonging to WIPO technical field 16 (which we shall call W16 patents), i.e. patents belonging to "Pharmaceuticals" within the 35-field WIPO classification. Then, we refer to the Orange Book (OB) in order to focus on patents that have yielded a new drug. The OB is a yearly publication of drug products, approved on the basis of safety and effectiveness by the Food and Drug Administration, containing related patent and exclusivity information. When not specified otherwise, the analysis in the remainder of the paper includes a concatenation of OB editions between 1985 and 2020. Fig. 1 presents a concise description of how new drugs are classified in the OB. The most relevant information for us is: trade or generic name: it defines the commercial product name; therapeutical equivalent code (TE): it defines whether a product is a therapeutical equivalent. TEs are distinguished under label 'A' ("Drug products that FDA considers to be therapeutically equivalent to other pharmaceutically equivalent products") and under label 'B' ("Drug products requiring further FDA investigation and review to determine therapeutic equivalence"); applicant to FDA: it represents the firm requiring approval which *does not* necessarily coincide with the original patent applicant.

Additionally, the section "Patent and exclusivity information addendum" allows to recover information on patent applications linked to drug applications submitted to the FDA. The Addendum contains patent and exclusivity information for the Prescription, OTC, Discontinued Drug Product Lists, and for the drug products with approval under Section 505 of the Federal Food, Drug, and Cosmetic Act, administered by the Center for Biologics Evaluation and Research (CBER), i.e. the Center within FDA that regulates biological products for human use under applicable federal laws.

Public funding information is retrieved from PatentsView which provides information on government interest statements in USPTO patents. The dataset allows to break down the source of funding among the various US public institutes (e.g. National Institute of Health, Department of Health and Human Services, etc.). Additional general information on patents, patent citations and the like come from PATSTAT.

Firm-level information is retrieved from Orbis IP, which provides a 10-year rolling window for firm balance-sheet data, and Compustat, which provides long-term figures for listed companies.

Fig. 2 presents a synthetic diagram of the analysis workflow, which also highlights relevant data sources and matching procedures.

## Patent data analysis: in search of the innovation crisis

In this section we present our empirical evidence on the purported crisis of innovation in the pharmaceutical sector. We will start by analysing the underlying quality of patents in the industry by means of standard patent quality indicators in Section 3.1. We then analyse the role of governmental agencies in funding private patents in Section 3.2 and look at the patterns of appropriability conditions by the dynamics of extended patent families in Section 3.3.

### *Quality indicators of pharmaceutical patents*

The PATSTAT database contains 177,040 W16 patents published since 1837, of which 171,743 (≈ 97%) published since 1968. Fig. 3(a) presents the long run trend since 1837 while Fig. 3(b) shows the ratio of W16 patents over all published patents in each year. The ratio stays roughly constant for the first 25 years of the XX century, grows approximately linearly between 1925 and 1975, and after that shows a roughly quadratic increase. This acceleration is a sign of the institutional changes that we have described in the introduction.

Of all pharmaceutical patents, 5655 (≈ 3.3%) are mentioned in the Orange Book (we shall call them OB patents). The time evolution of OB patents is presented in Fig. 4(a) while the ratio is shown in Fig. 4(b). Over time, the fraction of OB patents versus W16 patents does not present any remarkable steep trend. Fig. 4(c) shows that OB patents are predominantly pharmaceutical, but also cover related fields such as organic chemistry, medical technology, biotech, and the like.

What are those patents about? Tables 1 and 2 present a breakdown of the relevant

CPC technological classification codes at the 4-digit level for the two sets of patents (W16 and OB, respectively). In both cases, A61K ("Preparations for medical, dental, or toilet purposes") is the dominant CPC code, a code typically assigned to pharmaceutical inventions. It is worth noting that the W16 set presents a strong presence of process innovations (e.g. methods and apparatus to sterilise materials), while OB patents are essentially product innovations.

Unfortunately, we cannot distinguish between therapeutical equivalent products 'A' and 'B' for the whole set of OB patents, but restricting the analysis to only the latest release of the Orange Book (2021), which covers 3151 patents (≈ 56%) of the overall 5655 OB patents, we find that, among approved drugs, only 22 (≈ 3%) over 764 therapeutical codes are listed under the B category. Fig. 5 presents the cumulative distribution of trade names by patents. The top 20 trade names over a total of 988 distinct trade names (top 2%) are covered by approximately 10% of patents (388 of 3714). This number shows that therapeutical equivalent treatments are quite concentrated in a relatively small group of commercial products. Table 3 presents a list of the top 20 products with the number of related patents.

We now ask the extent to which these patents present an innovative content by matching them with some patent quality indicators used in the literature (Squicciarini et al., 2013). We will make reference to five patent quality indicators, that we consider particularly relevant in our case:

**Backward citations:** patent applicants are asked to disclose the prior knowledge which they have relied upon and, in particular, cite existing patents and scientific publications which their purported innovation is somehow indebted to. These citations are used to assess patentability and evaluate the legitimacy of the claims. The number of citations can help estimate the degree of novelty of an invention (Criscuolo and Verspagen, 2008). Backward citations, either to patents or to non-patent literature (NPL), are positively related to the value of a patent (Harhoff et al., 2003). However, many backward citations may signal a more *incremental* innovation (Lanjouw and Schankerman,

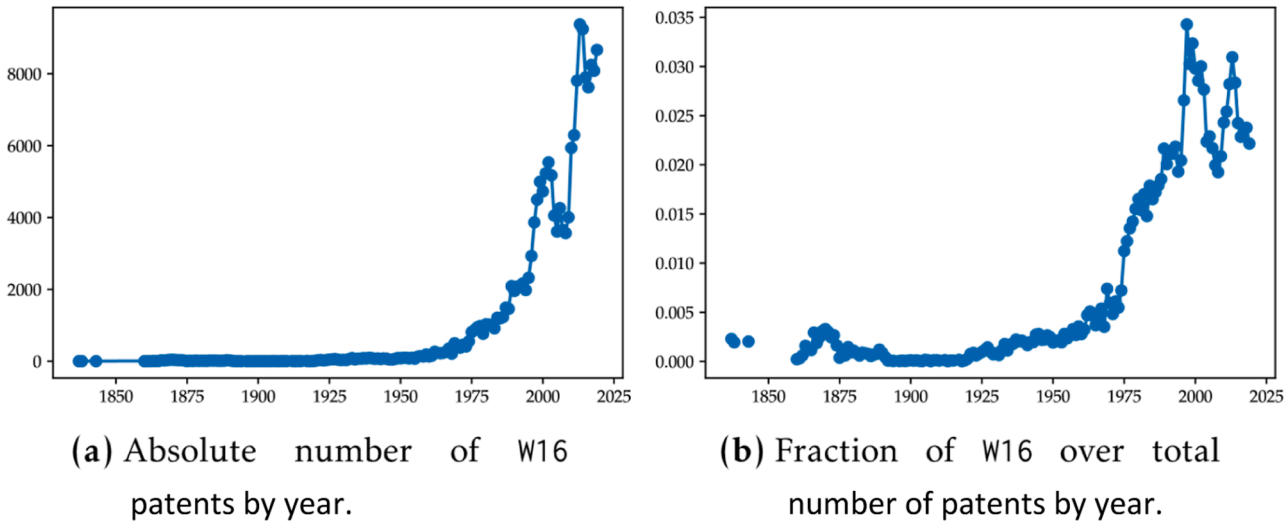



**Fig. 3.** Patenting activity in pharma (1837–2019).

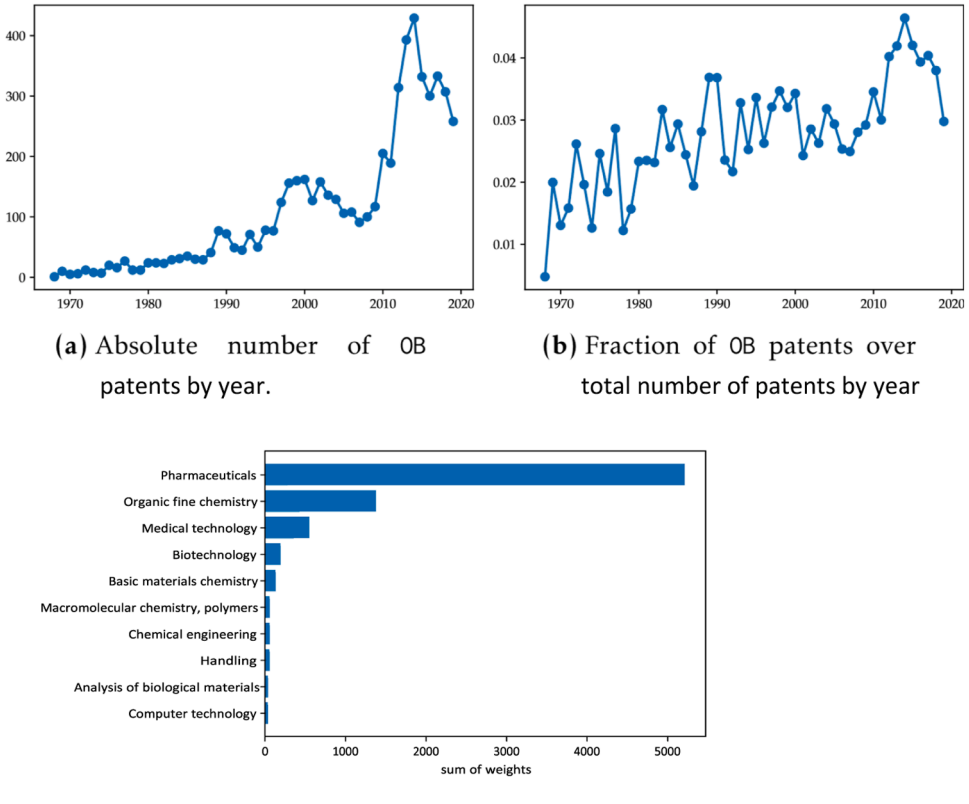



**Fig. 4.** Patents treating diseases (1968–2019).

2001). Our backward citations indicator excludes references to NPL, which is considered separately in our next indicator, and it does not particularly suffer from truncation error. Different technology fields share similar backward citation patterns, 5–10% of patents do not rely on prior art (i.e. they do not contain backward citations) and only a very small percentage of patent documents contain more than ten backward citations.

**Citations to non-patent literature:** backward citations to NPL can be considered as indicators of the contribution of public science to industrial technology (Narin et al., 1997). They reflect how close a patented invention is to scientific knowledge and help assess the proximity of technological and scientific development. Patents citing NPL tend to contain more complex and fundamental knowledge (Cassiman et al., 2008) and have significantly higher quality than patents that do not (Branstetter, 2005). NPL citations represent a subset of backward citations; as such, they do not suffer from truncation error. In the 1998–2009 period very few patents cite NPL. Sectors follow a very similar pattern, with most patents in all sectors not citing any NPL.

**Number of claims:** claims determine the boundaries of patent protection. The number and content of claims determine the breadth of

**Table 1**
Top 10 CPC codes within W16 patents.

| Code | Count | Definition |
|---|---|---|
| A61K | 598,309 | PREPARATIONS FOR MEDICAL, DENTAL, OR TOI-LET PU... |
| C07D | 126,946 | HETEROCYCLIC COMPOUNDS |
| C07K | 80,802 | PEPTIDES |
| C12N | 55,074 | MICROORGANISMS OR ENZYMES; COMPOSI-TIONS... |
| Y10S | 38,854 | TECHNICAL SUBJECTS COVERED BY FORMER USPC CROS... |
| C07C | 23,419 | ACYCLIC OR CARBOCYCLIC COMPOUNDS |
| G01N | 18,659 | INVESTIGATING OR ANALYSING MATERIALS BY DETERM... |
| A61L | 17,036 | METHODS OR APPARATUS FOR STERILIZING MA-TERIALS... |
| Y02A | 15,033 | TECHNOLOGIES FOR ADAPTATION TO CLIMATE CHANGE |
| A23L | 9346 | FOODS, FOODSTUFFS, OR NON-ALCOHOLIC BEV-ERAGES,... |

**Table 2**
Top 10 CPC codes within OB patents.

| Code | Count | Definition |
|---|---|---|
| A61K | 34,041 | PREPARATIONS FOR MEDICAL, DENTAL, OR TOI-LET PU... |
| C07D | 2831 | HETEROCYCLIC COMPOUNDS |
| Y10S | 1655 | TECHNICAL SUBJECTS COVERED BY FORMER USPC CROS... |
| A61P | 663 | SPECIFIC THERAPEUTIC ACTIVITY OF CHEMICAL COMP... |
| C07C | 591 | ACYCLIC OR CARBOCYCLIC COMPOUNDS |
| A61M | 509 | DEVICES FOR INTRODUCING MEDIA INTO, OR ONTO, T... |
| C07K | 408 | PEPTIDES |
| G01N | 398 | INVESTIGATING OR ANALYSING MATERIALS BY DETERM... |
| Y02A | 370 | TECHNOLOGIES FOR ADAPTATION TO CLIMATE CHANGE |
| A61J | 239 | CONTAINERS SPECIALLY ADAPTED FOR MEDICAL OR PH... |

IPRs. Patent fees are also based on the number of claims. Hence, the number of claims not only reflects the technological breadth of a patent, but also its expected market value (Tong and Frame, 1994, Lanjouw and Schankerman, 2001, Lanjouw and Schankerman, 2004). The indicator is defined as the number of claims per patent. Technology fields seem to vary in the average number of claims per patent. Caution should be used when making intertemporal comparisons because different averages might reflect different underlying distributions. For instance, biotech patents feature on average 22 claims per patent in 1999 and 13 in 2009, while the standard deviation is above 16 in 1999 and 12 in 2009; micro and nano-tech patents contain on average 20 claims in 1999 and only 12 in 2009, while the standard deviation drops from 17 in 1999 to 8 in 2009.

**Forward citations:** the number of citations a given patent receives is an indicator of the technological importance of the patent for the development of subsequent technologies. To a certain extent, they also reflect the economic value of inventions (Trajtenberg, 1990; Hall et al., 2005; Harhoff et al., 2003). Forward citations are counted over a period of five or seven years after publication and the count includes self-citations. The indicator is defined as:

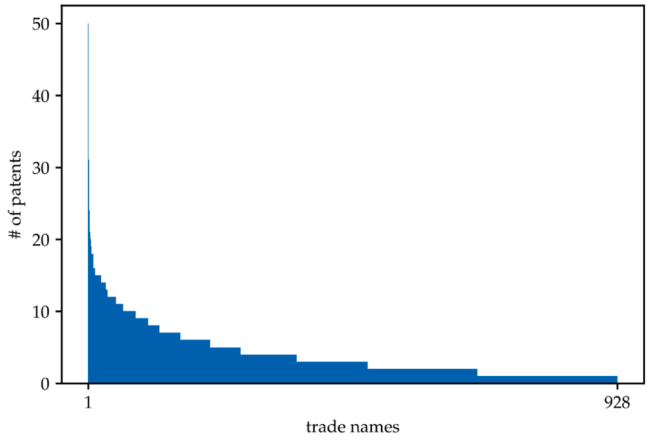



**Fig. 5.** Distribution of OB patents by trade name.

**Table 3**
Top 20 trade names and number of OB patents.

| Trade name | # patents |
|---|---|
| VASCEPA | 50 |
| IMBRUVICA | 31 |
| HYSINGLA ER | 24 |
| ESBRIET | 21 |
| GATTEX KIT | 20 |
| XIFAXAN | 19 |
| VIEKIRA XR | 18 |
| SYMDEKO (COPACKAGED) | 18 |
| VYVANSE | 18 |
| ORKAMBI | 16 |
| OSMOLEX ER | 16 |
| TRIKAFTA (COPACKAGED) | 16 |
| ENVARSUS XR | 16 |
| XTAMPZA ER | 15 |
| DSUVIA | 15 |
| BAFIERTAM | 15 |
| ZOHYDRO ER | 15 |
| BENDEKA | 15 |
| PENNSAID | 15 |
| OXYCONTIN | 15 |

$$CIT_{i,T} = \sum_{t=P_i}^{P_i+T} \sum_{j \in J(t)} C_{j,i} T \leq 5$$

$\mathrm{CIT}_{i,T}$ : number of forward citations received by patent application $i$ published in year $P_i$ within $T$ years from publication

$C_{j,i}$ : dummy variable that gets value 1 if the patent $j$ is citing patent $i$, and 0 otherwise

$J(t)$ : set of all patents applications published in year $t$

The forward citations index has generally decreased over time and there is substantial heterogeneity across technology fields.

**Breakthrough innovations:** breakthrough innovations are high-impact innovations which serve as a basis for future technological developments, new products, or new services (Popp et al., 2013) and are defined as the 1% most cited patents. Also in this case truncation occurs.

Fig. 6 presents the time evolution of the above mentioned quality indicators. Panels (a), (b), and (c) show the time evolution for W16, OB, and all patents in general, respectively. Each line shows a year-average taken across the population of interest (W16, OB, all patents). With respect to backward and NPL citations, the pharmaceutical sector, both overall and limited to OB patents only, presents a remarkable steep trend, by far more pronounced when compared to the set of all patents. Indeed, this evidence reflects the huge leverage the pharmaceutical sector does on both prior and scientific knowledge. Recall that while a high number of backward citations might signal quality because of the complex knowledge content embedded in patents, the latter can also be an indicator of more incremental innovation. The contribution of public science is instead a proxy of good quality, but also signals that a large body of knowledge appropriated by pharmaceutical patents relies on public scientific knowledge.

With reference to patent breadth, reflected by the number of claims included in each patent document, we observe that W16 patents have a stable trend in the number of claims, ranging from 10 to 15 across our time frame. However, OB patents present a higher number of claims, ranging between 15 and 25, in the period under analysis. Therefore, recalling that the number of claims represents a direct expression of the extension of appropriability, patents linked to drugs approved by the FDA have a remarkably higher breadth. Higher breadth is also reflected into higher forward citations that OB patents on average receive, reaching approximately 30 citations in 2015 (the declining trend after 2015 is affected by truncation).

In order to better appreciate the difference among our patent samples, Figs. 6(d), 6(e), and 6(f) plot, respectively, the ratios between OB and W16 patents, between W16 patents and patents in all technological

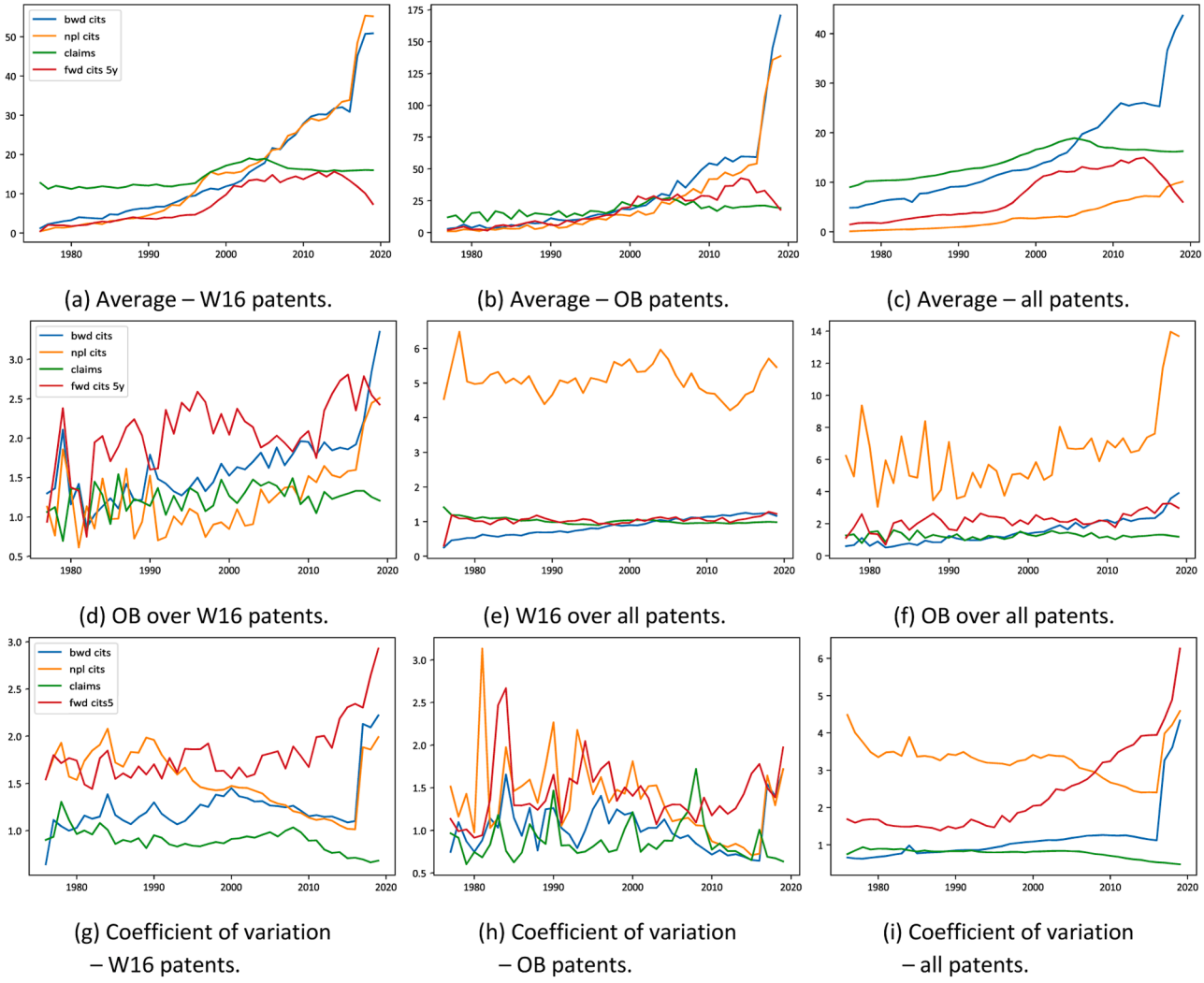



**Fig. 6.** Time evolution of quality indicators: yearly average (first row), relative (second row), coefficient of variation (third row).

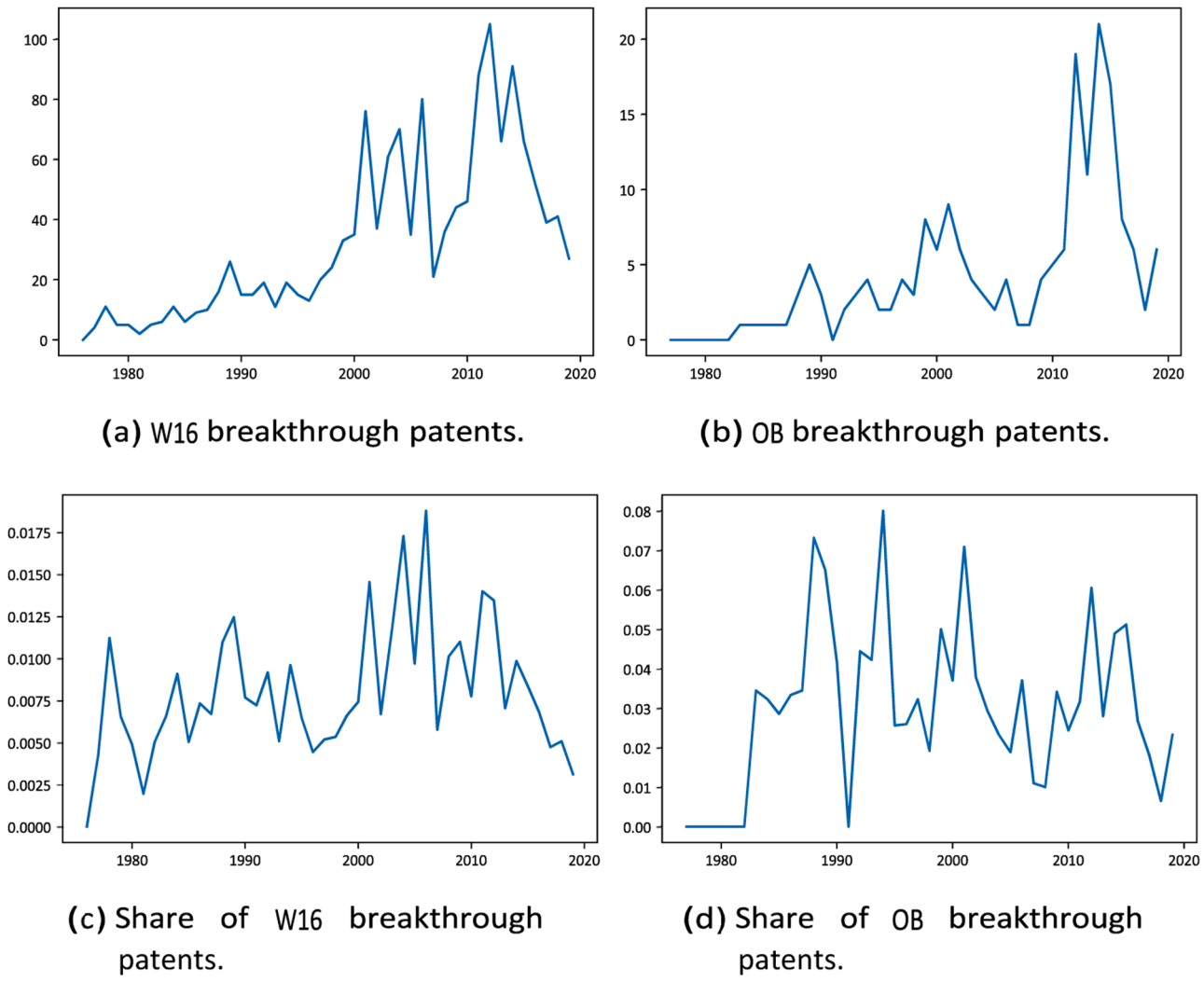



**Fig. 7.** Breakthrough patents (1968–2019).

fields, and between OB patents and patents in all technological fields. OB patents generally seem to display better quality compared to both W16 and all patents, especially in the two indicators of forward and NPL citations. The latter indicator is 5 to 8 times greater in pharmaceutical patents (with peaks in OB patents) than in the whole set of patents.

Figs. 6(g), 6(h), and 6(i) plot the coefficients of variation of quality indicators for the three sets of patents: W16, OB and all. Tracking variability across patents is important in order to detect heterogeneity. Regarding W16 patents, indicators which present a decreasing variation over time are backward and NPL citations (except the spike after 2015). At the opposite, forward citations present a strong divergent trend over time, signaling how the between-patent variation is quite remarkable. OB patents show instead approximately mean-reverting trends. Forward citations show the highest variability across patents over time.

Finally, panels (a) and (b) of Fig. 7 show the time evolution of the number of breakthrough patents, counting yearly the top 1% patents in terms of forward citations in the past five years, among all technological classes. In both sets, trends are increasing, however numbers are quite small, with peaks at 100 and 20 patents respectively. A more telling picture is presented in panels (c) and (d) of the same figure, where the ratio of breakthrough patents over total patents is dramatically low for

**Table 4**
Public funding agencies and number of W16 patents.

| Agency | # patents |
|---|---|
| Any agency | 14,312 |
| National Institutes of Health | 10,661 |
| National Cancer Institute | 823 |
| United States Government | 713 |
| Department of Health and Human Services | 652 |
| National Science Foundation | 537 |
| Department of Defense | 380 |
| Army | 369 |
| National Institute of Allergy and Infectious Diseases | 335 |
| Public Health Service | 308 |
| Department of Energy | 276 |

**Table 5**
Public funding agencies and number of OB patents.

| Agency | # patents |
|---|---|
| Any agency | 75 |
| National Institutes of Health | 47 |
| Department of Health and Human Services | 16 |
| National Cancer Institute | 10 |
| United States Government | 4 |
| Public Health Service | 4 |
| Department of Veterans Affairs | 3 |
| Army | 3 |
| National Institute on Ageing | 2 |
| National Institute of Mental Health | 2 |
| National Institute of General Medical Sciences | 2 |

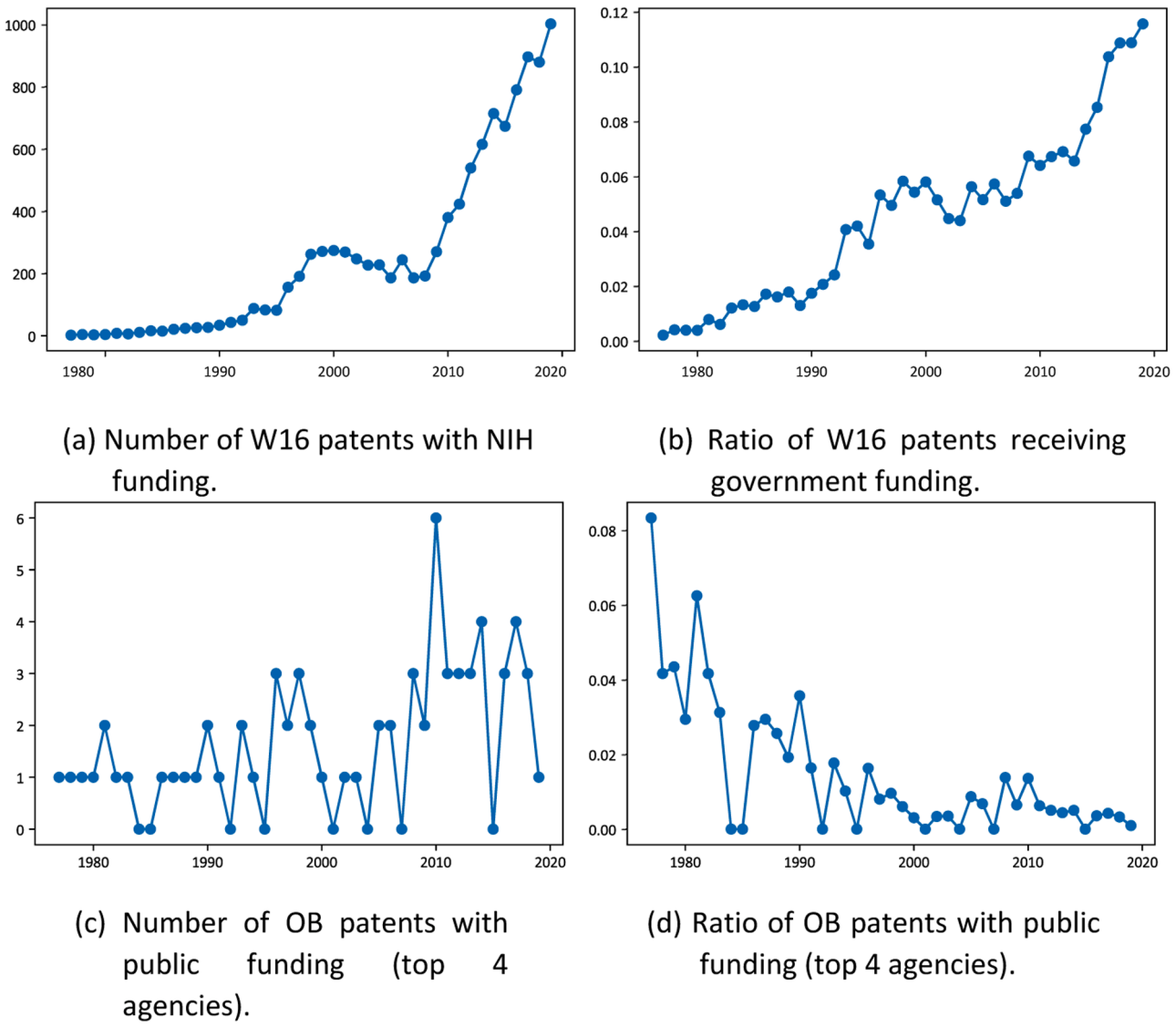



**Fig. 8.** Public funding of W16 patents (NIH only) and OB patents (top 4 agencies).

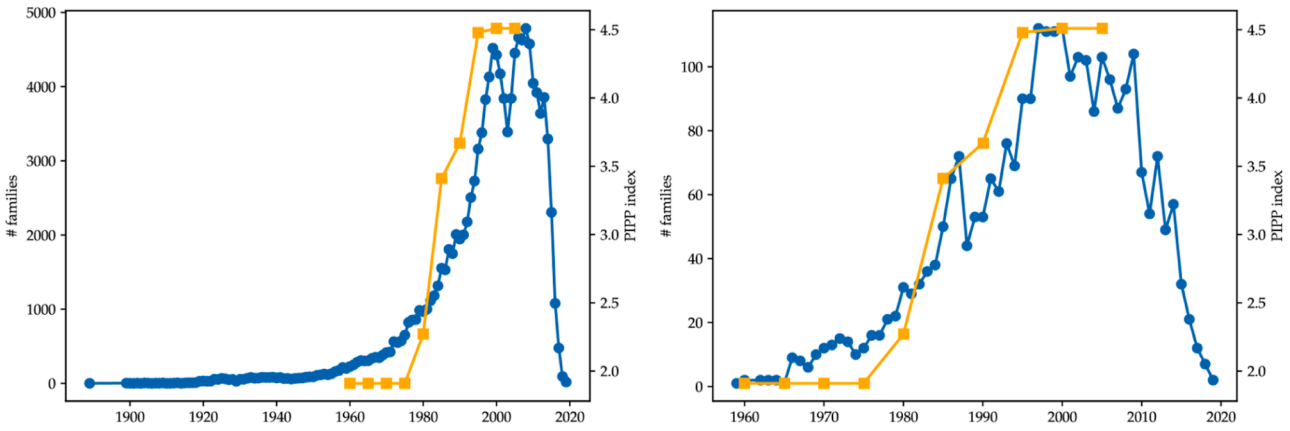
**Table 6**
Top 20 applicants (only listed companies) of OB patents receiving government interest.

| Applicant | # patents |
|---|---|
| MERCK | 7 |
| KALA PHARMS INC | 5 |
| SIGA TECHNOLOGIES | 4 |
| JANSSEN BIOTECH | 2 |
| ASTELLAS | 2 |
| AVID RADIOPHARMS INC | 2 |
| CELGENE INTL | 2 |
| LAB HRA PHARMA | 2 |
| JANSSEN PHARMS | 2 |
| PALATIN TECHNOLOGIES | 1 |
| LIFE MOLECULAR | 1 |
| ACROTECH | 1 |
| ALEXZA PHARMS | 1 |
| GENZYME CORP | 1 |
| FOLDRX PHARMS | 1 |
| CARDINAL HEALTH 414 | 1 |
| AZURITY | 1 |
| TITAN PHARMS | 1 |

W16, ranging from 0.2% to 1.75%, and notably with a declining trend since 2005. With respect to new drugs approved, the number of breakthrough patents, quite volatile because of small numbers, does not exceed 8%.

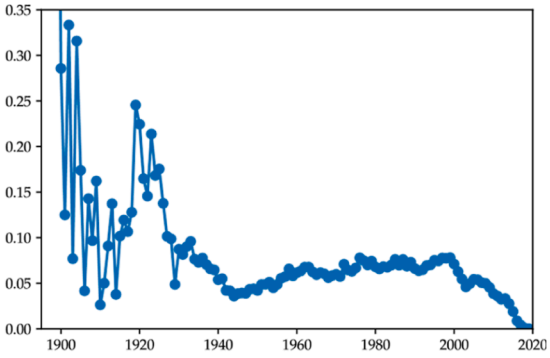
*Public funding*

We now turn to the role of public funds in the production of patented innovations. According to Light et al. (2005), Big Pharma has profoundly transformed its business model, devoting an ever declining fraction of expenditure to basic research. For example, with reference to so-called *neglected diseases* (e.g. a vaccine for HIV/AIDS, more effective diagnostics for tuberculosis, and better treatments for leishmaniasis and sleeping sickness) Moran et al. (2009) reports that public funding was responsible for 69% of total R&D expenditure. Garattini and Chalmers (2009) reports that public funding is taking care of the most-risky drug developments while Stevens et al. (2011) finds that 153 new FDA-approved drugs, vaccines, or new uses of existing drugs were discovered through research carried out in public-sector research institutions. Beyond the pharmaceutical sector, an increasing role of public institutions in guiding the discovery and innovation process has been documented looking at prize winning innovations (Block and




(a) Number of families by year with at least one W16 patent and PIPP index.

(b) Number of families by year with at least one OB patent and PIPP index.




(c) Ratio of new W16 families over existing W16 families.

**Fig. 9.** Extended patent families.

**Table 7**
Top 10 families per decade and underlying applicants (only listed companies) of W16 patents.

| | | | | | | | 1970s | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 483,109 (1973) | 627,642 (1972) | | 739,332 (1975) | | 495,087 (1976) | | 627,715 (1972) | 1,888,371 (1978) | 573,984 (1964) | 4,056,068 (1976) | | 473,664 (1969) | | 661,755 (1972) | | | | |
| Pfizer | 20 | Bayer | 18 | Roche | 17 | GlaxoSmithKline | 16 | Bayer | 13 Pfizer | 12 | L'Oreal' | 12 | Bristol-Myers Squibb | 12 | Merck | 11 | Procter & Gamble | 11 |
| Total | 21 | Total | 18 | Total | 25 | Total | 16 | Total 1980s | 16 Total | 14 | Total | 24 | Total | 12 | Total | 19 | Total | 12 |
| 508,242 (1980) | 514,555 (1984) | | 514,726 (1985) | | 320,415 (1985) | | 1,139,385 (1983) | 1,114,838 (1979) | 519,466 (1987) | 2,192,055 (1985) | | 320,133 (1984) | | 48,772 (1981) | | | | |
| Pfizer | 16 | Johnson & Johnson | 13 | Eli Lilly | 13 | GlaxoSmithKline | 13 | Pfizer | 12 | Merck | 11 | Regal Beloit | 10 | | | | | |
| Roche | 1 | Pfizer | 10 | Bristol-Myers Squibb | 9 | Sanofi | 9 | | | | | | | | | | | |
| Total | 18 | Total | 13 | Total | 16 | Total | 13 | Total 1990s | 12 | Total | 12 | Total | 29 | Total | 12 | Total | 19 | Total | 9 |
| 67,214 (1990) | 1430 (1992) | | 515,991 (1987) | | 5570 (1994) | | 159,598 (1988) | 1,271,007 (1992) | 41,529 (1988) | 1,230,319 (1989) | | 206,248 (1991) | | 160,568 (1992) | | | | |
| Ionis | 156 | Alnylam | 58 | Colgate-Palmolive | 32 | Roche | 26 | Stryker | 24 Pfizer | 25 | Roche | 22 | AbbVie | 21 | Nektar | 21 | Discovery | 19 |
| Novartis | 1 | Novartis | 1 | | | | | Curis | 2 | | | | | | | | | |
| Total | 483 | Total | 625 | Total | 54 | Total | 3205 | Total 2000s | 123 Total | 29 | Total | 40 | Total | 51 | Total | 70 | Total | 103 |
| 343,028 (1991) | 3196 (1996) | | 67,214 (1990) | | 5570 (1994) | | 4,990,278 (2005) | 987,885 (1997) | 47,842 (2002) | 41,211 (1998) | | 80,848 (2002) | | 1,029,037 (2000) | | | | |
| Eli Lilly | 57 | Perrigo | 32 | Ionis | 30 | Roche | 26 | Medtronic | 23 | Roche | 19 | Xencor | 18 | Becton Dickinson | 17 | Vyne | 15 | AbbVie | 15 |
| Total | 312 | Total | 122 | Total | 483 | Total | 3205 2010s | Total | 63 | Total | 42 | Total | 218 | Total | 136 | Total | 115 | Total | 18 |
| 37,701 (1997) | 337,472,490 (2010) | 4,848,881 (2001) | 405,123,419 (2011) | 66,176 (1997) | 47,842 (2002) | 414,841,034 (2013) | 459,187,117 (2015) | | 1,862,215 (2001) | | 406,608,378 (2011) | | | | | | | |
| Gilead | 110 | Johnson & Johnson | 97 | Neonode | 43 | Moderna | 43 | Conformis | 35 | Xencor | 31 | Sanofi | 29 | Axsome | 26 | Coherus | 25 | ThrapeuticsMD | 22 |
| Qualcomm | 1 | | | | | | | | | | | | | | | | | | |
| Total | 458 | Total | 138 | Total | 126 | Total | 189 | Total | 222 | Total | 218 | Total | 37 | Total | 48 | Total | 42 | Total | 62 |

Keller, 2009).

In order to detect forms of public funding in pharma patents we follow an alternative route: by means of the PatentsView dataset, we are able to identify the patents reporting some form of government interest. Tables 4 and 5 present a breakdown of W16 and OB patents reporting forms of public funding. Overall, we found 14,312 patents with public funding among all W16 patents, and 75 among OB patents. The National Institute of Health (NIH) provides by far the largest share of funding.

Fig. 8 summarises the main results. Panels (a) and (b) present the time evolution in the number of patents receiving public funding from the NIH and their ratio over all W16 patents. A steep increasing trend is quite visible, with NIH funding being present in 12% of pharma patents in 2019. Panels (c) and (d) present the corresponding patterns for OB patents where, given the small numbers involved, we consider not only NIH, but the top four funding agencies. Numbers are small and quite volatile, but the ratio shows a clearly declining trend. Table 6 presents the top assignees of patents receiving forms of government interest.

What can we infer from these two opposite trends? Considering the complementary evidence on the more prominent role played by the public funding in more risky and breakthrough research efforts (Moran et al., 2009; Garattini and Chalmers, 2009, Stevens, Jensen, Wyller, Kilgore.

*Appropriability*

The final piece of evidence we would like to add concerns the increasing similarity and decreasing innovative contents in newly released patents. Indeed, there are alternative ways to characterise similarity in patents, for example by looking at their technological classification. However, a quite straightforward but relatively unexploited piece of information comes from extended patent families.

According to the definition by the European Patent Office (https://epo.org/searching-for-patents/helpful-resources/first-time-here/patent-families/inpadoc.html) an extended patent family (also known as an INPADOC family) is "a collection of patent documents covering a technology. The technical content covered by the applications is similar, but not necessarily the same. Members of an extended patent family will have at least one priority in common with at least one other member – either directly or indirectly." Extended families differ from "simple" families, which generally track applications of the very same innovation to different patent offices. Indeed, extended patent families are useful to understand the applicants' strategy to gain patent protection on the basis of cumulativeness of inventions and patent thickets. Extended families are built by consolidating both direct and indirect priority links between patent applications within families. As a result, it is possible to find two patent documents with no priority in common, but which are indirectly related because they both share at least one priority with a third application (Martinez, 2011).

Although strong heterogeneity has been found in the dynamics of extended patent families, ranging from simpler (singleton) to complex structures, based on the country of origin of the applicant and on technological fields, analysis of temporal evolution of extended patent families by industry is still missing. In Figs. 9(a), 9(b), and 9(c) we present the long term evolution of newly entered families by year of observation, considering W16 and OB patents, and the ratio between new entries and the stock of existing families. The patterns show a long phase of technological diversification, during which new patents are assigned to new families, and a phase starting around 2000 in which technological diversification across patent classes seems to come to a halt. Indeed, the ratio between new entry and existing families shows two phases, one from 1940 up to mid 1990s with an increasing trend, and one from the 2000s onward with a declining trend.

In order to externally validate our measure of appropriability conditions, we compare the time dynamics of extended patent families versus the Pharmaceutical Intellectual Property Protection (PIPP) index developed by Liu and La Croix (2015), restricted for the US and available from 1965 to 2005. The index is an amelioration of the Ginarte and Park (1997) index and it is specifically constructed for pharma industry. It is a composite indicator of three sub-composite indices, namely, the Pharmaceutical Patent Rent Appropriation (PPRA) index, the Pharmaceutical Patent International Agreements (PPIA) index and the Pharmaceutical Patent Enforcement (PPE) index. Among the three indices, the first one is exactly meant to understand the types of pharmaceutical inventions that can be awarded a patent or be protected by another type of intellectual property right. Liu and La Croix (2015) identify five categories of products to measure the extent of patent rent appropriation, namely (i) new chemical entities; (ii) new pharmaceutical production processes; (iii) new medical indications for existing pharmaceuticals; (iv) new formulations of a medicine, e.g. new dosing schedule, new dosage form, new strength and new time-release variations; and (v) exclusive marketing rights and patent extensions for orphan drugs, biologics, and drugs tested on pediatric populations.

All these types of patent protections are granted by the US IPR system. Indeed, cases (3), (4), (5) are all possible sources for emergence and growth of extended patent families inasmuch they are linked to existing drug discoveries. For example, the so-called formulation patents (4) that cover improvements in existing products, such as new combinations, new dosage forms, new dosage schedules, and new dosage strength, are allowed in the US. The time correlation between extended patent families and the PIPP index, until 2005 (last available year of the IPPP) is quite evident in Figs. 9(a), 9(b).

More detailed information on the structure of patent families is provided in Tables 7 and 8 where we present for five decades (1970s, 1980s, 1990s, 2000s, and 2010s) the top ten families in terms of number of patents they collect, the top ten corresponding applicants among listed firms (again in terms of number of patents), PATSTAT family identifiers and their year of birth. The evidence for both W16 and OB patents shows decreasing concentration of families in terms of number of firms and increasing size in terms of patents: while in the first two decades many families were single-firm, with the top patent assignee holding almost the entire family, since the 1990s concentration has been declining. However, such higher diversification of families derives from a sizeable increase in the number of patents they collect. It is the case for example of family 5570 born in 1994, gathering 3205 patents with Roche, the top applicant, holding only 26 of them. Bigger extended families, collecting more distinct firms, signal over time higher technological proximity of inventions and increasing similarity. OB patents present smaller and more stable values over time.

## Firm-level analysis: appropriation, R&D expenses, and profitability

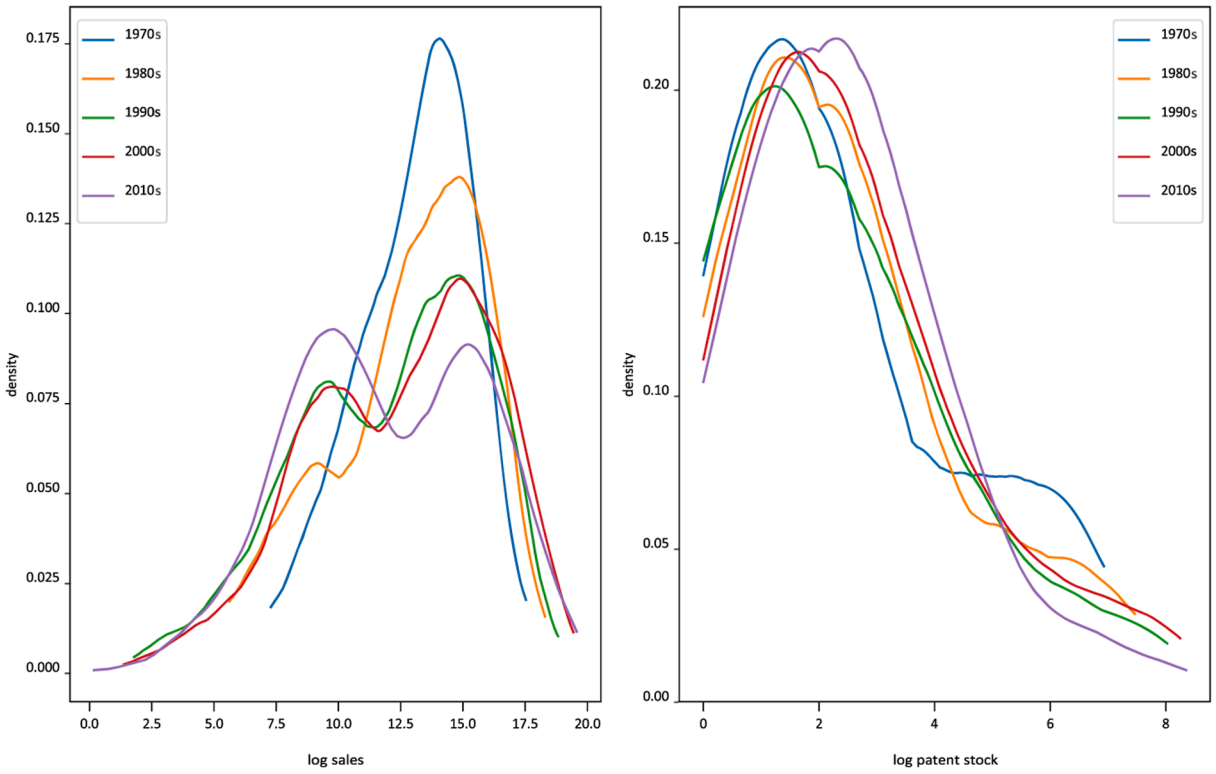
In this section we present evidence on indicators of firm-level corporate performances, focusing on patterns of R&D expenses and profitability of top patenting firms. Applicants are retrieved from Orbis IP and matched with Compustat via thicker identifiers of their global ultimate owner. Our database starts in 1950, although the majority of information is available from the 1970s. The purpose of the analysis is to detect the extent to which (i) R&D expenses reflect into patenting activities, (ii) patenting and profitability have a positive association. Due to data limitation on corporate performances, in the following we limit the analysis to the top ten patenting firms listed in Compustat, consistently with a "Big Pharma" analysis.

Indeed, before focusing on top patenting firms, it is important to understand the underlying dynamics of patenting activity by firm size. In Figs. 10(a), 10(b) we first plot the kernel density distributions of (log) sales of patenting firms and (log) patent stock by each decade. In this respect, we intend to detect the temporal evolution of size and patenting distributions. While the distribution of firm size shows a changing shape over time, with increasing dispersion and even bi-modality in the last two decades, the patent distribution is quite stable.

Table 9 splits the firm size distribution by quartiles, into bottom,

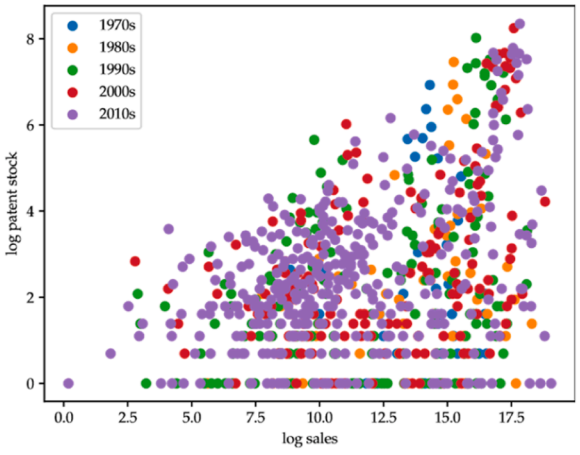
**Table 8**
Top 10 families per decade and underlying applicants (only listed companies) of OB patents.

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1970s | | | | | | | | | | | |
| 473,664 (1969) | 479,595 (1972) | | 49,269,939 (1970) | | 485,474 (1973) | | 476,712 (1970) | | 498,914 (1977) | | 752,270 (1966) | | 500,559 (1978) | 486,601 (1974) | | 473,491 (1970) | | |
| Merck | 11 | Johnson & Johnson | 7 | Johnson & Johnson | 6 | Eli Lilly | 4 | Bristol-Myes Squibb | 4 | Pfizer | 4 | GlaxoSmithKline | 4 | Eli Lilly | 3 | Eli Lilly | 3 | Pfizer | 3 |
| Total | 19 | Total | 9 | Total | 7 | Total | 4 | Total | 5 | Total | 17 | Total | 8 | Total | 3 | Total | 7 | Total | 12 |
| | | | | | | | | 1980s | | | | | | | | | | |
| 2,192,055 (1985) | 48,772 (1981) | | 498,914 (1977) | | 509,541 (1981) | | 186,476 (1979) | | 511,104 (1980) | | 983,135 (1984) | | 554,999 (1981) | 468,599 (1984) | | 1,182,369 (1986) | | |
| Pfizer | 10 | Sanofi | 9 | Pfizer | 7 | Johnson & Johnson | 6 | Sanofi | 6 | Eli Lilly | 4 | Pfizer | 4 | Bayer | 4 | Dow Chemical | 4 | Merck | 3 |
| Total | 12 | Total | 9 | Total | 17 | Total | 6 | Total | 14 | Total | 5 | Total | 9 | Total | 15 | Total | 9 | Total | 5 |
| | | | | | | | | 1990s | | | | | | | | | | |
| 67,214 (1990) | | 41,529 (1988) | | 206,248 (1991) | | 138,292 (1991) | | 1,233,491 (1990) | | 1,276,895 (1992) | | 1,290,911 (1993) | | 1,259,335 (1991) | 634,113 (1988) | | 468,971 (1992) | |
| Ionis | 156 | Roche | 22 | Nektar | 21 | GlaxoSmithKline | 15 | Teva | 12 | Alkermes | 10 | Bayer | 10 | Astra Zeneca | 8 | Novartis | 8 | Vertex | 8 |
| Novartis | 1 | | | | | | | | | | | | | | | | | | |
| Total | 483 | Total | 40 | Total | 70 | Total | 40 | Total | 19 | Total | 24 | Total | 10 | Total | 14 | Total | 14 | Total | 15 |
| | | | | | | | | 2000s | | | | | | | | | | |
| 67,214 (1990) | | 80,848 (2002) | | 1,335,994 (2996) | 64,475 (1995) | | 206,248 (1991) | | 25,322 (1996) | | 1,006,104 (1999) | | 1,015,414 (1998) | 359,007 (1999) | | 1,276,895 (1992) | | |
| Ionis | 30 | Vyne | 15 | Acrux | 10 | Nurix | 7 | Nektar | 6 | Bristol-Myers Squibb | 6 | Alkermes | 5 | Abbott | 5 | Mannkind | 4 | Alkermes | 4 |
| Total | 483 | Total | 115 | Total | 14 | Total | 18 | Total | 70 | Total | 21 | Total | 13 | Total | 12 | Total | 15 | Total | 24 |
| | | | | | | | 2010s | | | | | | | | | | | |
| 406,608,378 (2011) | 144,435 (2002) | | 328,538,385 (2009) | 413,597,801 (2012) | 276,781 (2002) | | 5160 (2004) | | 412,034 (2006) | 444,207,968 (2014) | 80,848 (2002) | 329,363,474 (2009) | | | | | | |
| TherapeuticsMD | 22 | | | | | | | | | | | | | | | | | |
| Qualcomm | 1 | Bristol-Myers Squibb | 16 | Amarin | 16 | Amarin | 16 | Mannkind | 15 | AbbVie | 15 | AbbVie | 15 | Thermo Fisher | 15 | Vyne | 14 | Vyne | 14 |
| Total | 62 | Total | 79 | Total | 25 | Total | 23 | Total | 71 | Total | 40 | Total | 74 | Total | 29 | Total | 115 | Total | 45 |




(a) Kernel density estimate of log sales distribution by decade. Epanechnikov kernel with bandwidth = 2.

(b) Kernel density estimate of patent stock (in log) by decade. Epanechnikov kernel with bandwidth = 2.




(c) Scatterplot of patent stock (in log) against log sales by decade.

**Fig. 10.** Firm size vs. patenting activity.

**Table 9**
Number of firms and stock of patents by decade and by quartile of log sales.

| Number of firms/Patent stock | 1970s | 1980s | 1990s | 2000s | 2010s | Total |
|---|---|---|---|---|---|---|
| **Bottom quartile** | 10/15 | 34/17 | 84/31 | 97/42 | 151/161 | 376/266 |
| **Middle quartile** | 98/152 | 101/209 | 166/708 | 193/836 | 273/1970 | 831/3875 |
| **Top Quartile** | 22/3157 | 53/5364 | 84/17,485 | 127/22,971 | 155/33,358 | 441/56,329 |
| **Total** | 120/3324 | 188/5590 | 334/18,224 | 417/23,849 | 579/35,489 | |

middle and top ones, in order to account for the number of firms and patents by each size class over decades. While the number of firms by quartiles looks to be more equally distributed, the patent stock is extremely driven by big firms located in the top quartile and this dynamics is persistent over time, meaning that there is no evidence of any specific time episode allowing to identify a temporal break. In addition, Fig. 10(c) presents the scatter plot between (log)sales and patent stock (in log), for each decade. Albeit there might exist big firms producing a tiny fraction of pharma patents, and this is due to the fact that non-pharma firms are included in the whole matched sample, small firms show a little contribution to the overall patent stock in all decades, while big firms are responsible for the majority of awarded patents. Granted such size-patenting relationship, we can now focus on the dynamics of top patenting firms in Big Pharma.

Table 10 presents descriptive statistics in terms of the top ten patenting firms, defined as the cumulative patent count, the number of patents and the ratio between patents over sales. Not surprisingly, such Big Pharma companies as Pfizer, Sanofi, Roche and GlaxoSmithKline appear among the top companies. Among the top ten patenting firms two strong outliers emerge: the first is Pfizer which presents a W16 patents over sales ratio much higher than the other firms. However, this anomaly of Pfizer tends to disappear when we consider the ratio between OB patents only and sales. The other outlier is represented by the company Ionis, which appears only among the top 10 firms in OB patents. This firm presents a ratio close to 0.3, which indeed signals a completely different corporate strategy: Ionis is a biotech company specialised in drug discovery and potentially a patent-vendor to other firms.

Fig. 11 shows the dynamics of corporate performances in terms of sales, EBITDA (Earnings Before Interest, Taxes, Depreciation, and Amortisation) and R&D margins, calculated as ratios over total sales. It is interesting to observe the impressive increase of sales, and the two distinct dynamics characterizing profitability and patenting ratios. Albeit profitability stands between 15% and 45%, with an approximative average of 30% in the whole period, the R&D ratio is quite smaller, ranging from 5% to 20%, with an approximate average value of 15%.

In order to understand the temporal variability of the between-firm heterogeneity we calculate the standard deviation among both EBITDA and R&D margins over time and plot results in Fig. 12. EBITDA margins show a remarkably decreasing trend over time, hinting at a pattern of increasing similarity across firms in terms of profitability. R&D margins instead show an increasing trend in terms of between-firm differences. Overall, the top ten patenting firms are more similar in their expenditure in R&D rather than in their profitability. The standard deviation of the OB set is highly influenced by the behaviour of Ionis.

How do R&D expenses map into the number of patents? Fig. 13 presents the correlation structure among the annual stock of patents, distinguishing between W16 and OB patents, and annual R&D expenses. Looking at the correlation structure among R&D levels and stock of patents (first row), in both sets we detect a quite remarkable correlation, but with considerable heterogeneity across firms. When looking at margins, a more telling figure, we confirm a positive correlation structure. However, we are not able to target the amount of R&D expenses devoted to each patent, but a simple stock-flow relation. In Fig. 14 we perform the same exercise looking at EBITDA.

To what extent are patents the result of innovative activities or rather a strategy to secure profits? We conclude our empirical investigation by presenting the distribution of the correlation coefficients, now including all firms since the 1950 for which we find data. Given that, as shown above, top patenting firms all present a strong correlation in terms of both R&D and EBITDA margins, the question is now the extent to which the same pattern can be found in all firms in the dataset, and also whether correlations in R&D differ from correlations in profitability.

In Fig. 15 we plot the histograms, restricting our analysis to those firms whose correlation coefficients are statistically significant ($p$-value $> 0.1$). Correlation in patents vs. profitability is by far more prevalent across firms than correlation in patents vs. R&D. First, firms presenting a significant coefficient between R&D margins and stock of patents are fewer (37/38) than those ones having a significant correlation in profitability (55/56). Second, the distribution is more concentrated in positive values in EBITDA margins rather than in R&D margins.

The evidence presented so far shows that both R&D expenses and profit margins are positively associated with the stock of available patents. However, patenting activity seems to be a firm strategy to secure profits more than being the result of R&D efforts.

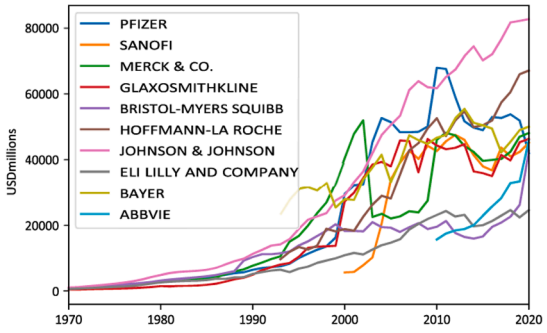
## Conclusions

In this paper we have attempted a comprehensive empirical analysis by matching complementary data sources on patenting activities in pharma. Notably, our paper represents one the few efforts linking new products included in the Orange Book and approved by the Food and Drug Administration with their patents.

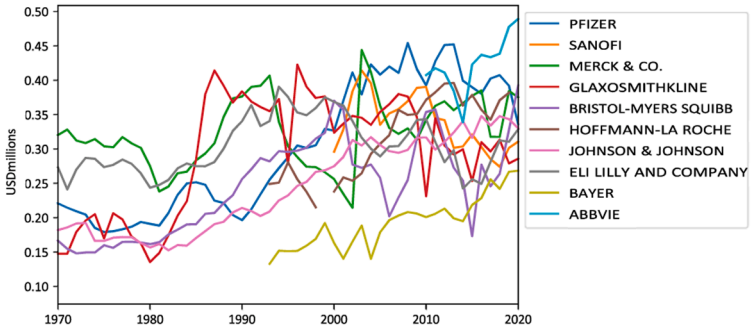
We analyse pharmaceutical patents along three main lines. First, we look at their quality by employing standard indicators in terms of backward and forward citations, citations to non patent literature, number of claims, breakthrough innovations. While pharma patents strongly rely on prior and scientific knowledge, the amount of breakthrough innovations is remarkably low and decreases over time. Second,

**Table 10**
Number of patents and patents/sales ratio of top ten patenting firms.

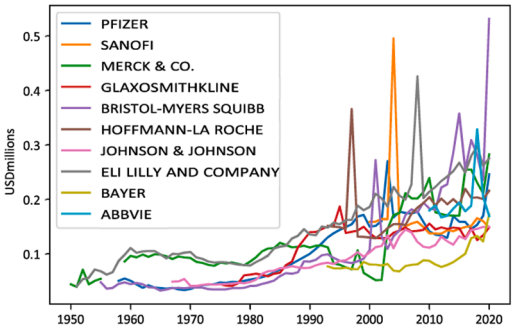
| W16 patents Company | # patents | # patents/last sales (m$) | OB patents Company | # patents | # patents/last sales (m$) |
|---|---|---|---|---|---|
| Pfizer | 4228 | 0.1 | Pfizer | 206 | 0.0049 |
| Sanofi | 2407 | 0.053 | Ionis | 205 | 0.2811 |
| Merck | 2276 | 0.047 | AbbVie | 197 | 0.0043 |
| GlaxoSmithKline | 2250 | 0.049 | Johnson & Johnson | 175 | 0.0021 |
| Bristol-Myers Squibb | 2152 | 0.051 | Merck | 131 | 0.0027 |
| Roche | 2116 | 0.032 | GlaxoSmithKline | 130 | 0.0028 |
| Johnson & Johnson | 1858 | 0.022 | Novartis | 128 | 0.0026 |
| Eli Lilly | 1832 | 0.075 | Eli Lilly | 122 | 0.0050 |
| Bayer | 1699 | 0.034 | Bristol-Myers Squibb | 120 | 0.0028 |
| AbbVie | 1411 | 0.031 | AstraZeneca | 119 | 0.0044 |




(a) Sales of top 10 patenting firms – W16 patents.

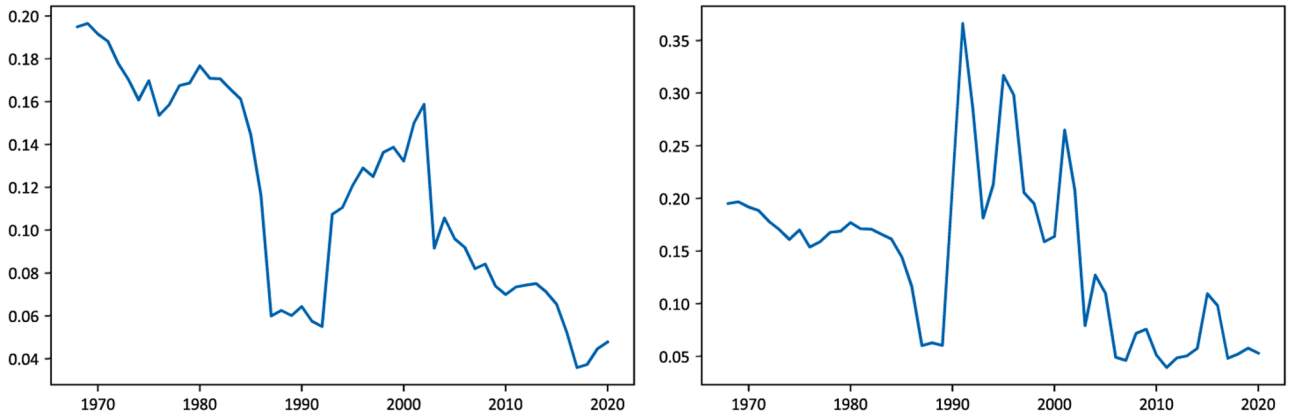



(b) EBITDA margins of top 10 patenting firms -W16 patents

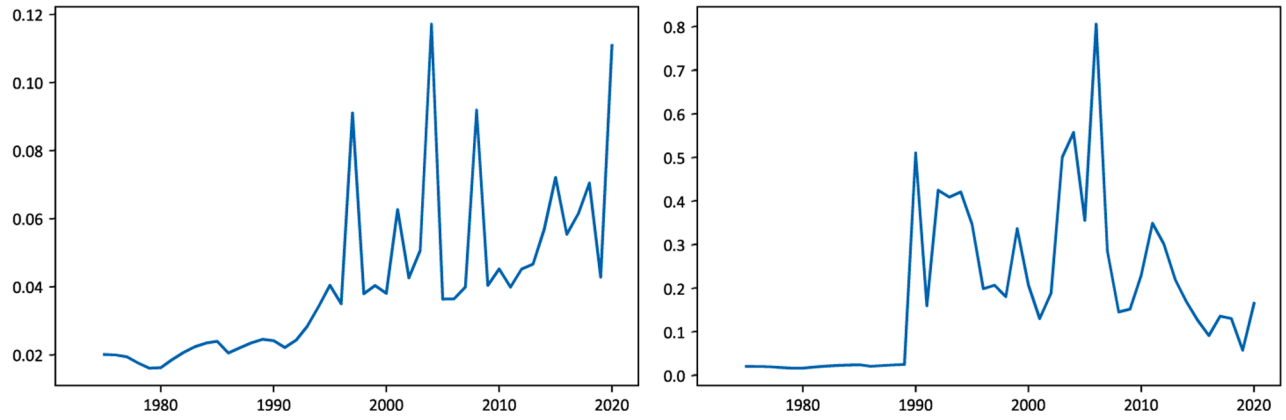



(c) R&D per sales of top 10 patenting firms – W16 patents.

**Fig. 11.** Number of W16 patents vs. corporate performance and R&D.

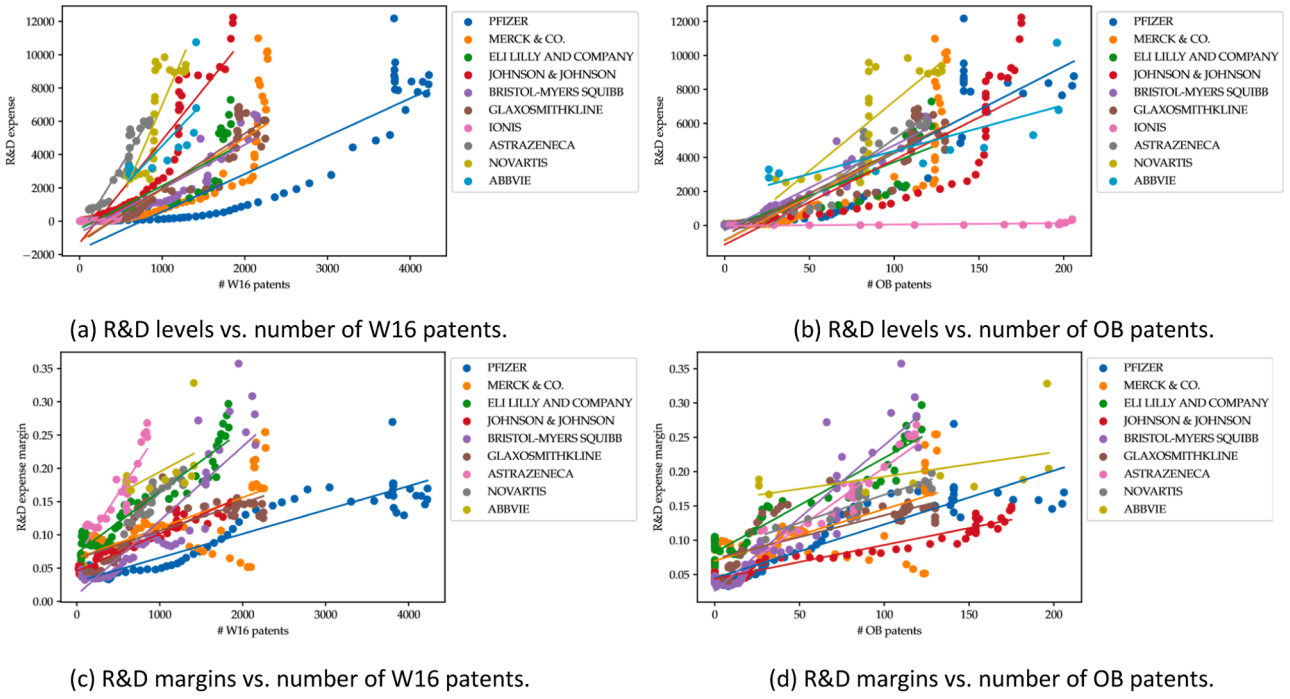



(a) Standard deviation in (b) Standard deviation in EBITDA margin – W16 EBITDA margin – OB patents. patents.




(c) Standard deviation in R&D (d) Standard deviation in R&D per sales – W16 patents. per sales – OB patents.

**Fig. 12.** Between heterogeneity in top patenting firms.



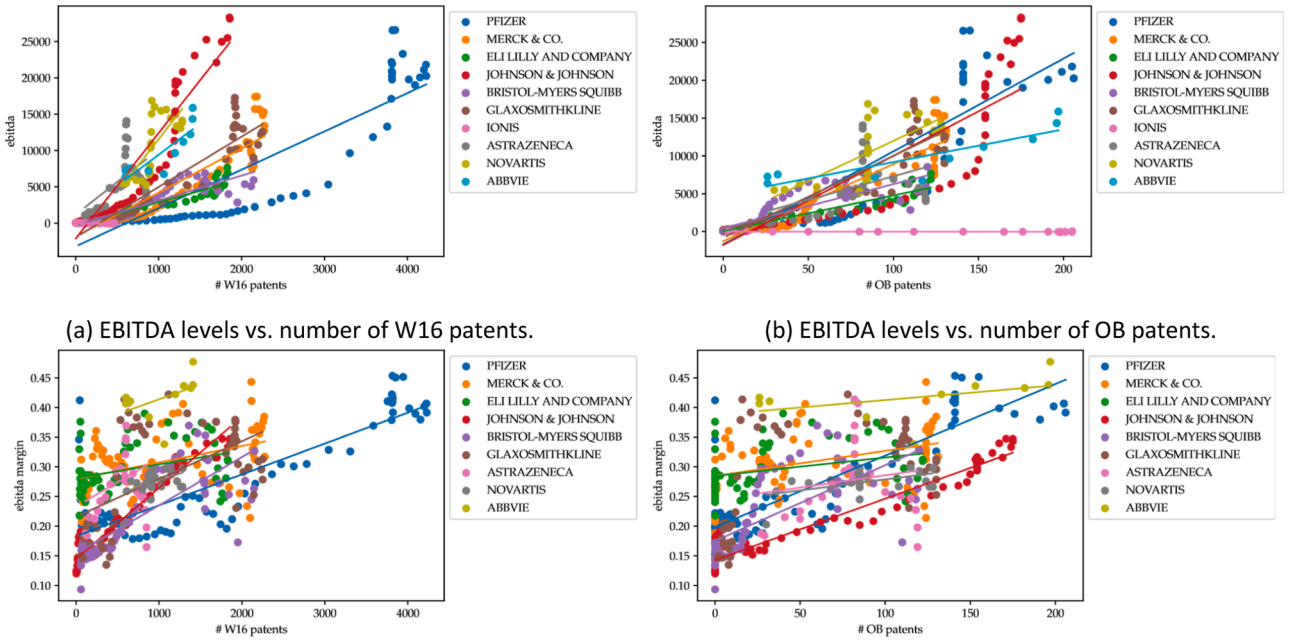

(a) R&D levels vs. number of W16 patents.

(b) R&D levels vs. number of OB patents.

(c) R&D margins vs. number of W16 patents.

(d) R&D margins vs. number of OB patents.

**Fig. 13.** Bivariate correlations: R&D expenses and patenting activity.



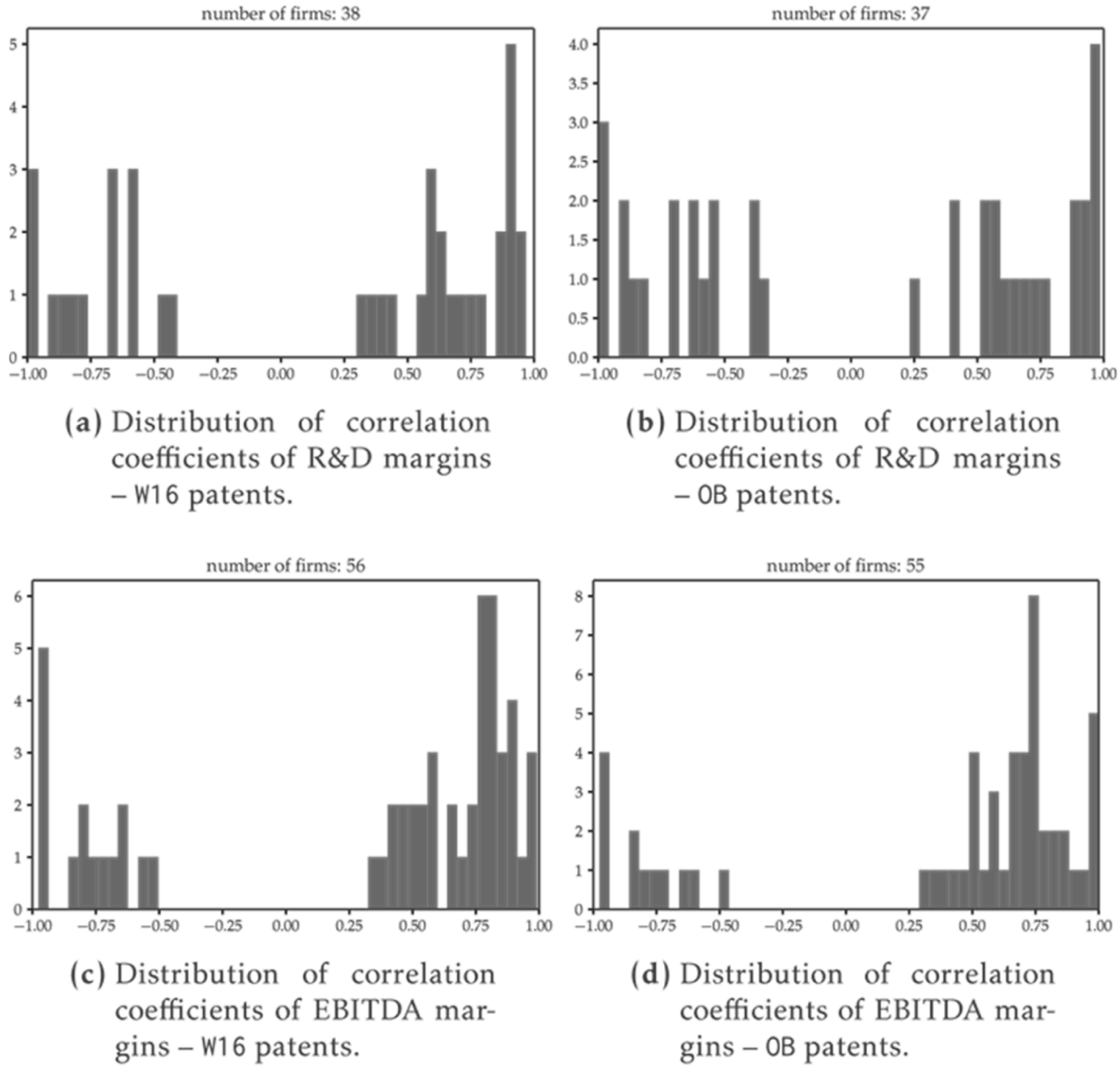

(a) EBITDA levels vs. number of W16 patents.

(b) EBITDA levels vs. number of OB patents.

(c) EBITDA margins vs. number of W16.

(d) EBITDA margins vs. number of OB.

**Fig. 14.** Bivariate correlations: profitability and patenting activity.




(a) Distribution of correlation coefficients of R&D margins – W16 patents.

(b) Distribution of correlation coefficients of R&D margins – OB patents.

(c) Distribution of correlation coefficients of EBITDA margins – W16 patents.

(d) Distribution of correlation coefficients of EBITDA margins – OB patents.

**Fig. 15.** Distribution of correlation coefficients .

we identify and characterise those patents receiving forms of government interest – as such a mark for quality – and find that OB patents are relatively few, decrease over time and concentrate on a bunch of products. Third, we look at appropriability via extended patent families and we identify a declining pattern of new families vis-à-vis the stock of existing ones, coupling with an increasing family size, signaling therefore raising patent thickets and stronger barriers to imitations.

After documenting that the big explosion in patenting activities does not map into a corresponding explosion in innovative activities, we move to the firm-level analysis in order to understand the relationship between patenting activities, profitability and R&D expenses. We document that top patenting firms present converging profit margins over the period of interest while between-firm R&D margins look to be diverging over time. Additionally, we find that R&D and profitability margins are quite correlated with the stock of owned patents for the top patenting firms while, when considering all companies, correlation in R&D margins reveals to be lower than the correlation in profitability.

Taking stock of the empirical evidence collected in this paper and considering the starting empirical question, whether IPRs are an institution promoting innovative activities, with reference to the pharmaceutical sector we can hardly support a positive answer. According to our analysis, IPRs encoded in patents represent legal barriers to protect

intellectual monopolies rather than an incentive and a reward to innovative efforts. Patenting strategies look to be quite aggressive in defining extensive knowledge borders and ample space of possibility of infringements.

Our results at the firm level are actually in line with other studies, conducted at the country level, which do not find a direct clear-cut effect of patenting activities upon R&D efforts. This is the case, for example, of the results in Qian (2007). Further developments of our line of research will entail the possibility of taking stock of the information-rich and newly constructed dataset in order to detect the extent to which institutional changes, like the Bayh-Dole Act or the increasing relevance of "*me-too*" drugs or formulation patents, might have played a role in reinforcing opportunities for rent appropriation. Even more important would be the study of the emergence of barriers to imitation constructed around the treatment of some specific diseases. An exemplary case is the AZT, synthesised as an anti-cancer in 1965, and then approved as a patent by the FDA in 1985 to cure HIV, commercialised as Retrovir in 1987 by Burroughs Wellcome (Liu and La Croix, 2015). Given that in the US patents do not only cover innovations but also "methods of use" as "new medical indications" and "methods of medical treatment", it would be very important to analyse the history of appropriability patterns enforced with respect to *neglected diseases*.

## Author statement

This paper is the product of collaboration among the authors on all parts and aspects of the paper and individual contributions cannot be determined.

## Conflict of Interest

The authors have no conflict of interest to declare.

## Data availability

Data will be made available on request.

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