



The sustainability of the health system and the pharmaceutical market: A permanent interaction between the cost of medications, the patent system, and disease care

La sostenibilidad del sistema de salud y el mercado farmacéutico: Una interacción permanente entre el costo de los medicamentos, el sistema de patentes y la atención a las enfermedades

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ABSTRACT Taking into account the latent threat of future pandemics, the objective of this study is to analyze – particularly with respect to medications – the sustainability of the health system, healthcare coverage, budgetary efficiency, and connections with the pharmaceutical patent system. In this context, the pharmaceutical patent system acts as a determining factor, given that promoting its existence stimulates the production of research, but in turn its existence stands in the way of rapid advancements, primarily due to the development of protective legislation concerning patents, which has largely accommodated the industry. Given that the pharmaceutical industry has managed to extend the duration of patents and avoid the incorporation of generics, our analysis focuses on the influence of pharmaceutical patents; this influence has led to reflection on the possibility of combining efforts by forging alliances between numerous companies and the public sector in order to face the challenges posed by new diseases caused by viruses that give rise to epidemics and pandemics.

KEY WORDS Health Systems; Patent; Health Policy; Investments; Drug Industry; COVID-19.

RESUMEN Ante la amenaza latente de futuras pandemias, este estudio tiene como objetivo analizar –desde el eje de los medicamentos– la sostenibilidad del sistema sanitario, la cobertura, la eficiencia del gasto y su vinculación al sistema de patentes farmacéuticas. En este marco, el sistema de patentes farmacéuticas adquiere un papel determinante, dado que fomentar su existencia estimula la producción de investigación pero, a su vez, su existencia no suscita un rápido avance, debido al desarrollo legislativo protector que han tenido las patentes y que ha dado lugar a un acomodamiento de la industria. Como la industria farmacéutica ha conseguido extender la duración de patentes y evitar la incorporación de genéricos, se analiza la influencia de las patentes farmacéuticas que ha dado lugar a reflexionar acerca de la posibilidad de consorciar esfuerzos realizando alianzas entre varias empresas y el sector público para afrontar los retos que plantean nuevas enfermedades producidas por virus que dan lugar a epidemias y pandemias.

PALABRAS CLAVES Sistema de Salud; Patente; Políticas de Salud; Inversiones en Salud; Industria Farmacéutica; COVID-19.

INTRODUCTION

Throughout the second half of the 20th century, the economic development-democracy dyad became the identifying characteristic of Western Europe. Nonetheless, the crisis of 1973, the end of the Bretton Woods system, the rise of neoliberal ideology under the political leadership of Ronald Reagan in the United States and Margaret Thatcher in the United Kingdom, and the fall of the Berlin Wall in 1989 have all cast doubt on the very existence of the welfare state, both ideologically and economically.

The distribution of increased social wealth achieved through the creation of public health systems, education systems, and pension funds led to gains in life expectancy at birth and improvements in other quality indicators, providing evidence of a correlation between economic development and income distribution. However, the issue of debt management has sparked debates over the sustainability of the health system, in particular with respect to the cost of drugs.

Patents form the basis for the pharmaceutical industry. Although the existence of patents and the protection of intellectual property motivate research and innovation, the system does not guarantee that new active substances will reduce healthcare costs or that new medications will unsustainably increase healthcare expenditures. Health is not exclusively dependent on the health system.

The theory of determinants of health – pioneered by Marc Lalonde⁽¹⁾ and Laframboise⁽²⁾ in Canada – has identified numerous factors that directly influence health: an individual's genetic background, aspects of lifestyle, environment, and the healthcare system a society possesses. This theory developed and improved upon existing explanatory models in the 1970s, which were progressively replaced with more complex models. What all of these models agreed on was that higher levels of per capita income in a society led to higher life expectancy.

The work of Whitehead, Dalhgren and Gilson⁽³⁾ has shown that not only does per

capita income influence a society's overall level of health, but that social inequality is also a determinant of health.

Doorslaer *et al.*⁽⁴⁾ analyzed the equity and redistributive effects of health systems in twelve OECD countries, along with their respective financing mixes. The authors concluded that health systems financed by the state through direct taxation have greater incidence in terms of their redistributive effect and impact on vertical inequity in favor of lower-income households.

Economic development is desirable because it brings with it greater social development, improvements in health, and a higher standard of living to all members of society. However, the work of Whitehead, Dalhgren and Gilson⁽³⁾ has opened up debates regarding the influence of social inequality on life expectancy, even in rich countries.

The impact of the pharmaceutical industry is crucial for rationalizing healthcare spending. The drug patent system is at the heart of the pharmaceutical industry, given that drug costs are connected to research costs. Pharmaceutical companies cover these costs exclusively through sales, within a price system that allows them to not only obtain a return on their investment, but also to remain profitable.

Public health crises such as A-H1N1, SARS2, and the current Covid-19 pandemic shake the foundations of several classical precepts. Rich countries have seen their health systems overwhelmed, despite having believed that they would no longer face high death rates due to infectious disease and that their primary objective was to keep chronic diseases in check. At the present moment, attention is directed toward two main issues: redesigning healthcare infrastructure in order to provide adequate care during the pandemic and returning to normal public health circumstances to foster a pharmaceutical industry that is capable of providing better solutions more rapidly.

From this perspective, this study aims to analyze – particularly with respect to medications – the sustainability of the health system, its coverage, spending efficiency, and

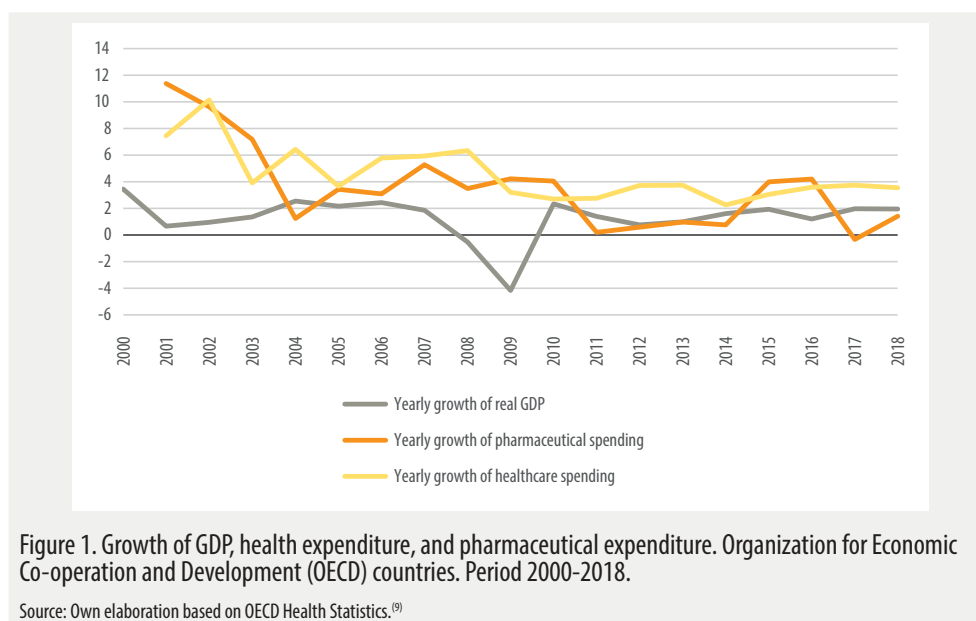
connections to the pharmaceutical patent system.

THE SUSTAINABILITY PARADIGM BEFORE COVID-19: NOT JUST A QUESTION OF SPENDING

The idea of sustainability has to do with protecting and meeting future needs by taking advantage of past resources. As such, research is a crucial component, given that no prevention would be possible without it. The concept of sustainability has several dimensions and can be approached from different perspectives; nonetheless, one of the more interesting elements for analysis has to do with identifying aspects related to system management that promote sustainability.⁽⁵⁾ Outlining strategies and economic prospects through a combination of economic, social, and public health analyses is a prerequisite for sustainability. In the last thirty years, debates have been permeated by considerations regarding the financial sustainability of the health system. Evidence has emerged that would seem to contribute to a tendency toward limitless growth in spending.

In OECD countries, health expenditure increased over the last third of the 20th century. In 1970, it represented on average around 5% of their Gross Domestic Product (GDP),⁽⁶⁾ and by 2018 it had risen to almost 9%.⁽⁷⁾ Nonetheless, limitless growth in public spending does not guarantee perpetual increases in life expectancy. Building on Samuel Preston's work from 1975 – which found a positive correlation between per capita income and life expectancy – Victor Fuchs⁽⁸⁾ popularized a version of this thesis: a curve showing that the positive relationship between healthcare expenditure and life expectancy only holds up to a certain point, beyond which the marginal effect of increased spending on improvements in health is practically nonexistent.

The Fuchs curve measures per capita health expenditure on the horizontal axis against life expectancy on the vertical axis. Fuchs'⁽⁸⁾ main finding was that increasing health expenditure is effective in developing countries, but not in rich countries. Wealthy nations have long debated how to slow the growth of healthcare spending. Figure 1 shows how growth rates of both healthcare spending and pharmaceutical spending have remained positive, even throughout most of the economic crisis.



The lack of a strategy based on the identification of health needs and the provision of a range of services intended to meet them can lead to malfunctions in the model. The comparison of pharmaceutical expenditure per capita and health expenditure per capita (Figure 2) shows that both have continually increased throughout the period analyzed. But what is even more alarming is that health expenditure is expected to surpass GDP growth in almost all OECD countries over the next 15 years. Health expenditure per capita will increase an average of 2.7% and is expected to reach 10.7% of GDP by 2030, compared to 8.8% in 2018.

The problem, therefore, is twofold: on the one hand, given the evidence, there appears to be no limit to growth in spending; and on the other hand, if the aim of the health system is to improve people's health, how to establish criteria to control spending while at the same time improving health production. But why has health expenditure continually increased despite diminishing marginal returns? The literature has pointed to three causes.⁽¹⁰⁾

The first is *growth in income level*. Empirical studies by Kleiman,⁽¹¹⁾ Barros,⁽¹²⁾ and Roberts⁽¹³⁾ have concluded that health expenditure is determined primarily by income

level. There are two theories that explain the correlation between per capita income and health expenditure. The first is based on the notion of health capital; that is, that improved worker health leads to increased productivity, and therefore increased opportunity cost of illness. The second is much simpler: higher-income countries have better educational and health levels.

The second is *increase in life expectancy*. Authors such as Zweifel⁽¹⁴⁾ and Okunade and Murthy⁽¹⁵⁾ have concluded that the principal determinant of health expenditure is the increase in life expectancy. James Fries⁽¹⁶⁾ formulated the "compression of morbidity" hypothesis, which states that as life expectancy increases, the onset of morbidity is postponed until closer to the age of death, with individuals enjoying more years of health rather than more years of illness.

The third is *technological innovation*. William Baumol's theory of the "cost disease" seeks to explain why improvements in technology do not necessarily lead to increased productivity in the healthcare sector.⁽¹⁷⁾

To date, the issue of sustainability has had a dual character. On the one hand, improved external sustainability, which has to do with not only finding ways to slow the

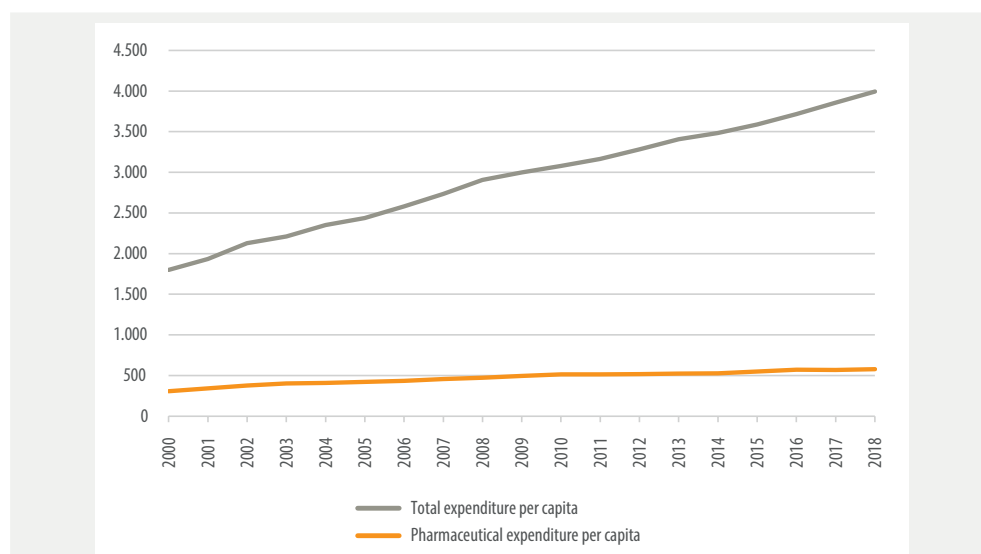


Figure 2. Per capita health expenditure and pharmaceutical expenditure. Organization for Economic Co-operation and Development (OECD) countries. Period 2000-2018.

Source: Own elaboration based on OECD Health Statistics.⁽⁹⁾

growth in spending, but also how to do so without bringing about negative effects in people's health. This involves determining the maximum amount of resources a society should allocate to its health system; or to put it another way, determining the point at which the marginal productivity of increases in health expenditure is equal to the marginal utility for the society's health. This requires deciding on a basic range of services and making a larger decision regarding the type of protections warranted by each healthcare need.⁽¹⁸⁾ On the other hand, internal sustainability depends on improved governance of the health system, adequate management of available resources, cost-benefit analyses of both technological innovations and spending increases, and overcoming the inherent inefficiencies in the health market.

A relationship between healthcare costs and system sustainability certainly exists.⁽¹⁹⁾ The search for a better use of resources has spurred an international movement known as the "Triple Aim," centered on providing better care and better health at a lower cost. As Mas and Wisbaum⁽²⁰⁾ describe it:

The *Triple Aim*, a term coined by Don Berwick, Tom Nolan, and John Whittington in 2008 [...] involves the following three goals [...] 1) Improving the patient experience (better care). 2) Improving the health of the population (better health). 3) Reducing the per capita cost of health care (lower cost).

Therefore, it can be said that health depends less on how much is spent and more on how it is spent.

TOWARD A NEW PARADIGM

The temporary shift in priorities due to the public health emergency brought on by Covid-19 will likely have repercussions for decades to come. Chronic diseases will no longer be front and center, as new viruses and more harmful mutations will cause

traditional debates to be eschewed. Table 1 shows the growth of Covid-19 cases in Spain; in less than one month the number of deaths increased by a factor of 75.

The universal coverage of Spain's health system assumes that each individual not only protects their own health but also the health of all other members of the community. The breakdown or weakening of healthcare coverage is a global public health issue that goes beyond considerations of economic redistribution.

It is clear that society must prepare for future pandemics. Aggressions against nature, food culture, and the number of people in extreme poverty – coupled with globalization – generate new diseases and cause them to spread to every continent. Covid-19 will not be the last, but rather will most likely be the first of many. However, it will not be possible to maintain overblown health systems with resources remaining idle when not being collapsed by a public health crisis, given that this would represent an unsustainable use of resources.

Research and production of new vaccines and medical treatments is not only a local issue, nor is it limited to the private sector.

The pharmaceutical market

With respect to the relations between agents in health markets, significant information asymmetries between physicians and patients produce market failures, which ultimately determine the concrete demand for services and procedures. Roles are disarticulated, creating a complex system of misaligned interests: the agent rendering payment – that is, the taxpayer through the state – does not make decisions; the consumer (patient) does not bear the cost of the service; and the decision-making agent (the physician) neither pays nor consumes.⁽¹⁰⁾

This lack of alignment causes patients to exert pressure such that their "felt need" is addressed, which does not always coincide with a "normative need," generally defined by experts.⁽²¹⁾ Furthermore, along with the

Table 1. Covid-19 cases. Spain, March 14 to April 8, 2020.

Date	New confirmed cases	Total confirmed cases	New active cases	Total active cases	New recovered	Total recovered	New deaths	Total deaths
14-3	1,100	6,332	697	5,603	324	517	60	193
15-3	1,512	7,844	1,432	7,035	0	517	99	292
16-3	2,098	9,942	2,035	9,070	13	530	50	324
17-3	1,236	11,178	589	9,659	498	1,028	149	491
18-3	2,591	14,769	3,391	13,050	53	1,081	147	638
19-3	3,308	18,077	3,087	16,137	26	1,107	195	833
20-3	2,333	20,410	1,616	17,779	481	1,588	210	1,043
21-3	4,964	25,374	4,629	22,408	537	2,125	335	1,378
22-3	3,394	28,768	2,401	24,272	450	2,575	394	1,772
23-3	4,321	33,089	3,280	28,798	780	3,355	410	2,182
24-3	6,584	39,673	4,385	33,183	439	3,794	514	2,696
25-3	7,937	47,610	5,626	38,809	1,573	5,367	738	3,434
26-3	8,578	56,188	6,278	45,087	1,648	7,015	655	4,089
27-3	7,871	64,059	4,757	49,844	2,342	9,357	769	4,858
28-3	8,189	72,248	4,429	54,273	2,928	12,285	832	5,690
29-3	6,549	78,797	3,287	57,560	2,424	14,709	838	6,528
30-3	6,398	85,195	3,515	61,075	2,071	16,780	812	7,340
31-3	9,222	94,417	5,894	66,969	2,479	19,259	849	8,189
1-4	7,719	102,136	3,467	70,436	3,388	22,647	864	9,053
2-4	8,102	110,238	3,056	73,492	4,096	26,743	950	10,003
3-4	7,472	117,710	2,770	76,262	3,770	30,513	932	10,935
4-4	7,026	124,736	2,511	78,773	3,706	34,219	809	11,744
5-4	6,023	130,759	1,489	80,262	3,861	38,080	674	12,418
6-4	4,273	135,032	1,278	81,540	2,357	40,437	637	13,055
7-4	5,478	140,510	1,964	83,504	2,771	43,208	743	13,798
8-4	6,180	146,690	610	84,414	4,813	48,021	757	14,555

Source: Own elaboration based on data from the Center for the Coordination of Health Alerts and Emergencies, Ministry of Health, Government of Spain.

benefits obtained by physicians who charge by service provided, or who simply seek to improve their image in the eyes of the patient by attending to their felt need, physicians and patients form an alliance against the state in its role as insurer-payer, who faces significant difficulties in controlling the volume of spending derived from millions of micro-level diagnostic and therapeutic decisions.

A consequence of this is the well-known alliance against the payer. Physicians want

to incorporate more technology – even though medications and procedures may be extremely costly – and patients aim to transform their felt needs into “met needs.” This leads to what has become known as the medicalization of discomfort –in some cases it has even been called disease mongering – which refers to professional and industrial actors inflating the demand for pharmaceuticals, equipment, or nutritional supplements in order to treat mild conditions, alongside

Table 2. Proposed hierarchical model of the right to health according to a typology of needs..

	Individual harm	Social harm	Economic harm
Reinforced protection	Life Harm	Spread of disease	Economic ruin Collapse
Custodial protection	Discomfort	Social disinvestment Alarm	Inequity
Selective protection	Difficulty	Deception	Inconvenience

Source: Gómez and Repullo⁽¹⁸⁾.

advertising campaigns that attempt to medicalize any and all discomfort. Furthermore, the allure of sophisticated technology increases the utilization of expensive (though less effective) styles of clinical practice because they are seen as innovative.⁽¹⁰⁾

The issue at hand is how to determine when the treatment of a disease should be covered with taxpayer money without taking into consideration its social value (for example, having the latest technology in a small local hospital). Gómez and Repullo⁽¹⁸⁾ propose a typology of health needs and their articulation of different levels of protection. This typology is summarized in Table 2, which outlines different healthcare settings and specifies the minimum content of the right to health protection. It also attempts to characterize health needs by proposing a hierarchy of levels of need according to the type of harm involved (individual, social, or economic), connecting them to a minimum level of essential coverage.

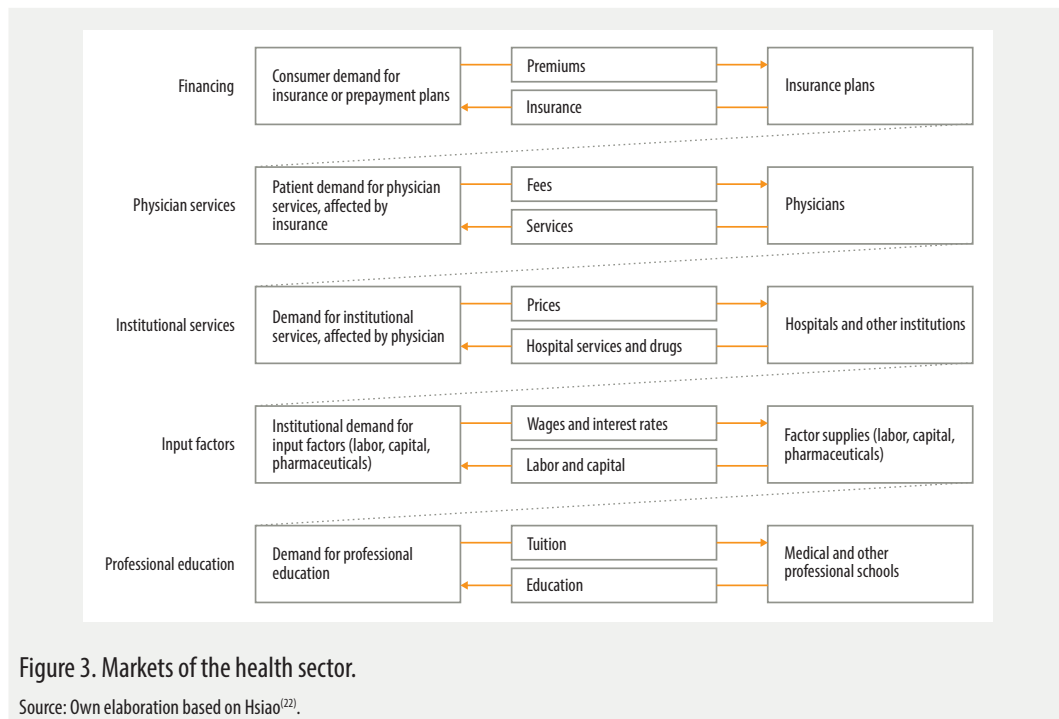
The highest level of coverage is *reinforced protection*, which comprises needs that involve serious threats to individual life, social protection from the spread of disease, and economic harm associated with the inability to pay for treatment. *Custodial protection* also refers to an unalienable level of protection, wherein the Legislature must demonstrate the absence of need in order for coverage to be withdrawn. In a similar but opposite manner, in the case of *selective protection* – the weakest level of protection – lawmakers must demonstrate proof of need.⁽¹⁰⁾

This hierarchy would distinguish between a newly released high-priced biopharmaceutical that does not offer improved effectiveness and another group of drugs whose use is justified, or one that is not directed to a health need that falls under the category of either reinforced or custodial protection.

Relatively uncommon or rare diseases can lead to premature death or to high morbidity, but due to their low incidence the pharmaceutical industry may have had little incentive to develop drugs to treat them. Drug production requires administrative support, which to date has primarily taken the form of research funding, simplified approval processes, and market exclusivity.

These high costs generate a tension between the sustainability of the system and notions of social justice, considerations that necessarily go beyond strictly economic analyses. Many medical decisions are made from a utilitarian point of view, but this does not guarantee that socially just criteria are taken into account. Furthermore, the health market is a prismatic space composed of multiple submarkets corresponding to different specialties. Hsiao⁽²²⁾ identifies five markets in the health sector that interact with each other, as shown in Figure 3.

As a supplier in the input factor market, the pharmaceutical industry is more tightly regulated than other productive sectors because it is a strategic market with a range of specialties. Its importance stems from two aspects: first, it represents a major cost to the system; and second, along with other inputs, the effectiveness of its products determines



the capacity and the efficiency of the system as a whole. If the pharmaceutical industry makes progress toward developing new medications that provide quicker and more effective cures, it will alleviate the rest of the system. The pharmaceutical product market has direct repercussions on the sustainability of the system in three ways: the volume of purchases in the system as a whole, the prices of these purchases, and the health benefits associated with new active substances, which improve health and ease the demand on healthcare infrastructure.

From a demand perspective, inefficiencies can be derived from the following: a) the provider, the payer, and the consumer are all different agents, which may lead to misaligned interests, as previously mentioned. b) Asymmetrical information can produce relations of agency. Consumers do not possess the knowledge to determine if expert indications are appropriate. This is one weakness related to drug copayments; since the consumer is not in charge of the decision, their demand is rigid in relation to the price of a

prescribed drug. As a consequence, copayments only have an effect on certain income groups, to the point that certain individuals with a normative need may be unable to access the medication they require. Some authors⁽²³⁾ have studied the effects of what is known as “supplier-induced demand.” c) The inelastic demand for prescription drugs. d) Price fixing occurs through negotiations that do not entirely respond to market allocation, although the state does not fully behave as a monopsony. e) Disease mongering and the medicalization of discomfort and of generally mild conditions is encouraged by the pharmaceutical industry and accepted by experts who seek to attend to felt needs. In order to avoid overprescription, price-volume agreements might be effective, in which a price is fixed for a determined sales volume, and the price goes down if sales exceed this volume.⁽¹⁰⁾

From a supply perspective, the most significant costs in drug production are those related to research and commercialization, given that the cost of producing the chemical

compounds themselves is relatively low. It is difficult to precisely determine the production costs of pharmaceuticals, as it is not always possible to distinguish between necessary and unnecessary costs or attribute them to a single product, as several authors have noted.^(24,25,26) Patents are granted in order to remove deterrents associated with externalities; however, precisely determining the magnitude of these costs is no simple task. The company holds a monopoly as long as the patent is in effect, permitting a higher price to be charged than would be the case with market competition; nevertheless, prices do not respond to the monopoly equilibrium point, given the administrative negotiation process. Moreover, the conflict between professionals and the pharmaceutical industry is especially relevant with respect to the incorporation of costly and ineffective drugs. Incorporating new parameters such as the drug effectiveness in order to set prices could prove useful in this regard.

Pharmaceutical patents

Patents are instruments that grant exclusivity rights to the laboratory that develops a drug, barring competitors from producing the patented drug for a period of 20 years.⁽²⁷⁾ In legal terms, patents are applied as a protection to the proprietary rights of the companies and individuals that develop new technology. From an economic standpoint, they seek to resolve externalities that lead to market failures when property rights are not clearly defined.

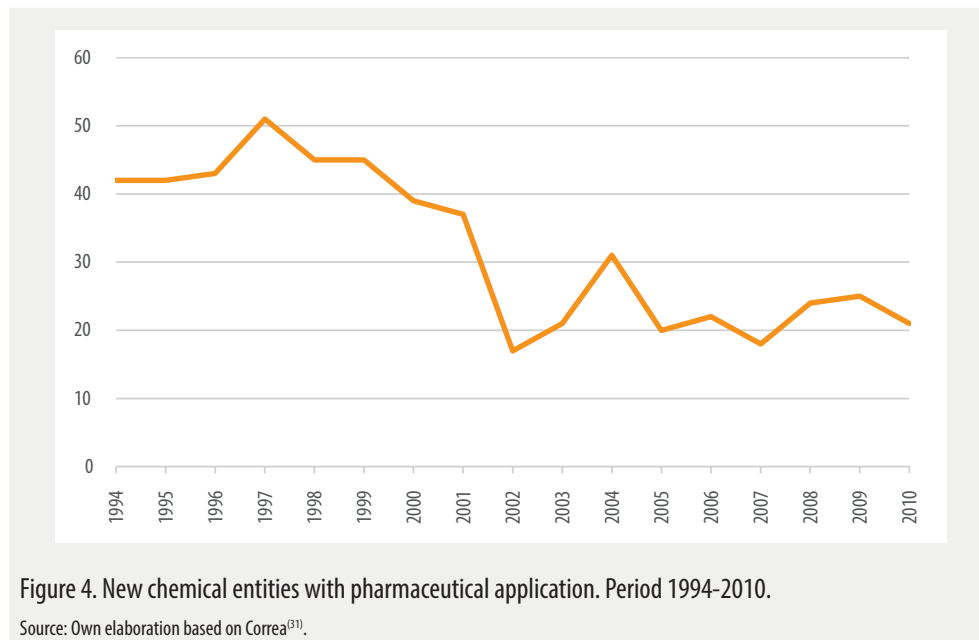
In the pharmaceutical sector, issues of equity must be considered alongside regulatory concerns seeking to optimize the distribution of costs and benefits. This is due to the fact that the application of patents and licenses – particularly in developing contexts, but also in richer nations – causes drug prices to be prohibitively expensive for some and generally unbearable in terms of system sustainability.

Parra Cervantes⁽²⁸⁾ classifies patents for active substances into six categories:

- a. *Molecule patent*: The most important category, it protects a chemical compound.
- b. *Synthesis patent*: The protection also extends to production temperature and conditions.
- c. *Process patent*: Protects physical and chemical modifications.
- d. *Formulation patent*: Protects from combination with other excipients common in pharmaceutical practice.
- e. *Drug interaction patent*: Results from combined effect of different drugs.
- f. *Method of use patent*: For when a different therapeutic use for a drug is found.

Regarding their characteristics, process patents are relatively weak protection mechanisms, as minor changes to procedures can provide a loophole. In developed countries there has been a historical tendency toward the progressive strengthening of the protections offered by patents, along with the evolution of the product patent. In Spain, for example, becoming a member of the European Community drove the 1986 patent law toward monopoly, with the introduction of product patents.

On July 8, 2009 the European Commission published the *Executive Summary of the Pharmaceutical Sector Inquiry Report*,⁽²⁹⁾ which called attention to abuses regarding competition in the pharmaceutical industry. In particular, it examined the misuse of patents for the purpose of impeding competition and maintaining monopoly prices. The report shed light on the market concentration taking place in the pharmaceutical sector, alongside the paradox of more patents and less innovation, as a reaction to the entry of generic drugs to the market. That is, pharmaceutical companies increase the number of patents based on minor modifications to a single product in order to avoid the entry of generics.⁽²⁹⁾ European economic thought is built upon the idea that competition is beneficial to society, and as such companies that attain a significant market share are closely monitored. In actuality, striking a balance between promoting corporate growth and limiting market power proves complex. Therefore,



Article 102 of the Treaty on the Functioning of the European Union⁽³⁰⁾ punishes the abuse of economic power, which is defined as the abuse of a dominant position within a particular market.

In this sense, two contentious practices emerge in the context of European antitrust law in the pharmaceutical sector. On the one hand, a practice is considered prohibited when it meets three material assumptions: 1) that a dominant position exists; 2) that it is abused; or 3) that it affects trade between Member States.⁽²⁷⁾ On the other hand, strategies to delay the entry of generic drugs, such as obtaining secondary patents – which may be granted based on different dosage forms, production methods, or specific pharmaceutical formulations – are employed when a patent is sought for a minor modification to a profitable drug, even when no new replacement product exists. These techniques are known as *blanketing* when referring to procedure patents, *flooding* when multiple patents are taken out for the same product, and *fencing* when certain lines of investigation regarding a particular product are blocked. They produce three main outcomes:

1. They raise administrative costs and increase litigation aimed at enforcing patents, and therefore raise product prices. The European Commission report⁽²⁹⁾ shows that the number of litigation cases increased by a factor of four from 2000 to 2007, even though generic companies won 62% of cases.
2. They limit innovation in the pharmaceutical sector. The tendency to seek stable conditions by minimizing the number of competitors affects not only administrative costs, but also scientific advancement. In a study on pharmaceutical patents in Argentina, Brazil, Colombia, India, and South Africa, Correa⁽³¹⁾ contrasts the decline in the development of new chemical agents between 1994 and 2010 (Figure 4) with the increase in the number of patents for simple modifications to existing drugs. However, this would not have been expected taking into account three factors: the application of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which allowed companies all over the world to increase revenues; the substitution of mass detection methods for

new drugs with more advanced methods such as genomics and proteomics; and the pharmaceutical industry's high levels of profitability in comparison with other sectors. To be sure, more resources are mobilized, fewer new products are obtained, and large firms remain dependent on small biotechnology companies and subcontractors specialized in clinical trial services. Perhaps the root of the issue lies with the crisis of the current model for new drug development. Correa's⁽³¹⁾ previously mentioned study found that each country had different patentability standards, and in those with stricter standards – with the exception of patents granted for minor modifications to existing products – more innovative products were developed.

3. They impede significant savings by delaying the entry of generic drugs to the market. The previously cited European Commission report⁽²⁹⁾ estimated that this led to the loss of three billion euros over the course of the seven year study period. The report stated that generic companies enter the market with prices that are 25% lower, and two years after entry prices are on average 40% lower.

Regulation of pharmaceutical patents

The discovery of new drugs that cure or alleviate the effects of disease is no simple matter. Pharmaceutical companies invest large amounts of resources and carry out numerous clinical trials until they are successful in finding a new active substance. In order to provide an incentive in the search for new drugs that will improve the health and well-being of society, patents are granted for 20-year periods.

The history of patent law can be traced back to the middle of the 19th century, and has developed in a similar fashion in different countries. Some relevant milestones include:

- 1844. France, which granted product patents for chemical substances, becomes the first major country to eliminate product patents in the pharmaceutical industry with a law passed on July 5.
- 1877. The first unitary law in Germany limits protection to production processes.
- 1907. Switzerland introduces process patents to its legal system with a law passed on July 21.
- 1919. The British patent system incorporates patent protection for specific production processes of chemical substances, replacing the formerly established protections to the substances themselves. Pharmaceutical patents were later weakened through compulsory licensing regulation. Previous conditions were not restored until 1949 (Patents Act of 1949) and 1977 (Patents Act of 1977).
- 1967. Germany admits product patents with a law passed on September 4, and a few months later France follows suit with legislation passed on January 2, 1968.
- 1970. The Patent Cooperation Treaty is signed on June 19, 1970 in Washington, creating the International Patent Application.
- 1973. The Munich Convention on European patents – the Convention on the Grant of European Patents (European Patent Convention)⁽³²⁾ – is signed on October 5, establishing an office for handling patent applications and incorporating reinforced procedure patents and product patents for drugs. In a rather roundabout manner, Article 52.4 allows for the patent of pharmaceutical products for a period of ten years, plus five additional years if requested by a State (Art 167.2 EPC).
- 1975. European Community Patent. Regulated by the Luxembourg Convention signed on December 15, 1975 (Luxembourg Conference on the Community Patent),⁽³³⁾ this contrasts with the previous agreement by establishing a unified and indivisible patent based on the principle of free movement of factors.⁽³⁴⁾
- 1977. Switzerland authorizes product patents.
- 1978. Italy becomes a paradigmatic case: having witnessed an unparalleled development of its pharmaceutical industry under patent prohibition, it had become one of

- 1844. France, which granted product patents for chemical substances, becomes the first major country to eliminate product

- the leading producers and exporters of intermediate products. However, a Supreme Court ruling on March 20, 1978 allowed patents to be granted in the industry.
- 1994. The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)⁽³⁵⁾ – signed on April 15 in Marrakesh at the culmination of the Uruguay Round negotiations – groups the results of intellectual property into two main categories: the protection of trademarks and distinctive features and the protection of innovations, designs, industrial models, and trade secrets. The balance between efficiency and equity that the World Trade Organization sought to achieve in the TRIPS agreement has three main aspects: 1) encouraging innovation with the presumption that future benefits will be perceived by the inventor; 2) encouraging technological transfer through the study of the patented discovery, in that the patent protects the property rights associated with the invention for its duration, but represents a point of departure for scientific advancement once it expires; and 3) making exceptions to property rights in situations of national emergency (TRIPS Article 27).⁽³⁶⁾

The agreement confers exclusive rights to the owner (TRIPS Article 28), but also provides for some exceptions – such as the so-called “Bolar” provision – assuming that they do not unreasonably conflict with the normal exploitation of the patent (TRIPS Article 30) or compulsory licensing (TRIPS Article 31). For example, this would allow manufacturers of generics to use these products without the patent owner’s authorization in order to produce generic versions of the drug that can be marketed as soon as the patent expires.

In the case of *Canada – Patent Protection of Pharmaceutical Products*, in their March 17, 2000 report, the Special Panel made one of the few official statements regarding the scope of Articles 30 and 31 of the TRIPS agreement.⁽³⁴⁾ As the admitted exceptions were ambiguous, the African Group and other World Trade Organization countries demanded clarification and proposed a special TRIPS Council meeting on the issue. The underlying concern

had to do either with the spread of HIV/AIDS on the African continent or the controversy in Brazil surrounding its 1996 Intellectual Property Law, among other possibilities.

Community provisions

Currently, Directive 2001/83/EC⁽³⁹⁾ of the European Parliament regulates this process. The process is initiated with local authorities and a marketing authorization is requested for the drug in question. In order to obtain authorization, the soliciting party must present clinical results (Article 8), a detailed bibliography documenting the medicinal efficacy of the drug wherever possible (Article 10.1.ii), and show that the drug is not essentially similar to other medicinal products that have been authorized (Article 10.1.iii).

Marketing authorization is valid for five years and is renewable for five-year periods (Article 24). There exists a mechanism governed by Regulation 469/2009⁽⁴⁰⁾ of the European Parliament, which states that patent owners can extend the duration for a maximum of five years (Article 13). The rationale for this stems from the fact that a significant amount of time elapses from the moment in which a patent is obtained until marketing authorization is granted. Known as Supplementary Protection Certificates (SPCs), this mechanism was created to offset that loss of time that the product can be on the market.

In Spain, the Industrial Property Statute (*Estatuto de Propiedad Industrial*, or EPI) had prohibited the patenting of “pharmaceutical or medicinal formulas” (Article 48.2 EPI), but the 1986 Law on Patents lifted that prohibition, although its entry into force was postponed until October 7, 1992 (First Transitional Provision).

Such legislative shifts must be understood in the context of Spain’s process of integration into the European Community. Spain pledged to accede to the European Patent Convention (EPC) in accordance with Protocol Number 8 of the Act of Accession to the Treaty. In fact, the Law on Patents reproduces the cited provision verbatim from the EPC.

In order to update this legal framework, new legislation was passed – Law 24/2015⁽⁴²⁾ – although it did not go into effect until April 1, 2017. The objectives outlined in the legislation include an interest in improving innovation, adapting marketing procedures, and strengthening the security of the concession system. The new law provides three forms of protection for the pharmaceutical industry: 1) it gives a clearer definition of what is understood as a patentable invention; 2) it regulates utility models; and 3) it explicitly includes Supplementary Protection Certificates.

The National Trade Association of the Pharmaceutical Industry estimates that investment in R&D totaled €1,147,497 in 2017. Industry spokespersons have traditionally held that without enhanced protection of intellectual property, the pharmaceutical sector would be forced to reconsider its levels of investment in R&D.

New models for the protection of research discoveries

The sustainability of the health system depends on healthcare coverage – which refers to both the range of services and benefits that society receives – and cost-efficiency in covering health needs. The pharmaceutical market, therefore, is central to the sustainability of the system. Historically, patents have been employed to resolve the issue of research. However, the development of a more protective legal framework through patenting has created other problems; for example, industry actors have adapted to these circumstances and have endeavored – often successfully – to extend the duration of existing patents and avoid the entry of generic drugs, with reduced outcomes in terms of innovation and new active substances.

This problem is far from encountering a solution. The question of what type of relationship should exist between the industry and healthcare authorities therefore remains open, and can be addressed through three issues. First, how to choose the most appropriate mechanism to correct for the positive

externalities produced by research, such that the costs involved in developing new drugs can be covered while still providing incentives to generate new products. Second, regarding financing decisions related to the development of new drugs, which ones should be financed, and to what degree. And third, in order to control pharmaceutical spending, healthcare authorities have incorporated measures such as reference prices, negative drug lists, or support for generic drugs.

Denying that the pharmaceutical industry is a key player in the discovery and innovation of new drugs would be just as mistaken as denying the industry's underlying profit motive. Therefore, the regulations of healthcare authorities are the only instruments that can effectively address failures in efficiency and equity in a market where the resolution of positive externalities can generate significant equity issues. Rather, public intervention must be designed as a “win-win” situation, where all involved parties satisfy their expectations or at the very least minimize their dissatisfaction. Moreover, the experience of the past 30 years has shown that a new paradigm is needed.

Entirely eliminating patent monopolies is unrealistic, as the industry maintains that they are a top priority, although some researchers question whether or not they are a prerequisite for technological and industrial development in the pharmaceutical sector. Furthermore, the elimination of mechanisms protecting industrial property would be debatable in the context of market economies of developed societies. Therefore, health policy should explore methods of introducing mechanisms to encourage research and innovation that guarantee economic success of the industry. Previous attempts to create ideal circumstances for the discovery of new drugs that would increment the health capital of society have had only one effect: the growth in profitability obtained by pharmaceutical companies without showing any signs of significant achievements in scientific advancement.

Until now, proposals to encourage the marketing of new drugs have centered on five strategies:

1. New value-based payment models.⁽⁴³⁾
2. Risk sharing agreements established between healthcare authorities and the pharmaceutical industry. The need for this stems from the difficulties associated with predicting drug effectiveness, given that they are developed through clinical trials in conditions that may differ from real situations of day-to-day clinical practice. In such arrangements, the price of a drug is not only linked to the number of units sold,⁽⁴⁴⁾ but a system of payment by results is also established – connecting with effectiveness and efficiency – such that the costs of a drug and the risk associated with its effectiveness are shared by the health system and the pharmaceutical industry. This allows for a return on investment, contributing to the sustainability of the system.⁽⁴⁵⁾
3. Buying power of public administration (monopsony). Controlling drug prices is a legal competency of the state.⁽⁴⁶⁾
4. Biosimilar and generic drugs. Generic drugs represent around half of total pharmaceutical sales volume across OECD countries.⁽⁴⁷⁾ The OECD report “Health at a Glance 2019”⁽⁴⁸⁾ states that increased use of generics can generate significant cost-savings.
5. Indication-based pricing.

These new models and proposals assume the existence of oligopolies in which balance is sought between industry profits and healthcare needs. However, the Covid-19 pandemic has demanded a distinct premise: international collaboration and shared research. The discovery of an individual scientist from anywhere in the world can become known to the international scientific community on the very same day, but fragmented clinical trials do not take advantage of magnitudes of scale, as knowledge is multiplied exponentially when it is shared. In the words of WHO Director-General Tedros Adhanom:

The first vaccine trial has begun, just 60 days after the genetic sequence of the virus was shared [...] This is an incredible achievement. We commend the researchers around the world who have come together to systemically evaluate experimental therapeutics, but multiple small trials with different methodologies may not give us the clear, strong evidence we need about which treatments help to save lives.⁽⁴⁹⁾

A difficulty arises with the allocation of property rights that correspond to each involved party, but if the model for international cooperation regarding research findings related to the pandemic is effective, it should contribute a formula that can be extrapolated to other pathologies, as it may be able to grant profitability to some research costs, especially with respect to diseases whose prevalence is low.

According to Marovac,⁽⁵⁰⁾ preclinical studies, animal toxicology studies, and regulatory review committees can last from three to five years, while Phase I trials can last from two to five years. Phase II trials – which can take from two to five years – are carried out with small cohorts in order to identify adverse reactions and to determine the minimum and maximum tolerable dose; one-third of molecules do not pass this stage. Phase III, which can last from two to four years, multiplies the number of patients involved in the trials by a factor of ten, and once again about one-third of drugs is rejected.⁽⁵¹⁾ Cutting down on the amount of time in Phases II and III is essential for reducing costs. Approval and registration with regulatory agencies can go on for anywhere from one to 25 years.

In 1960, the development of a drug took about 8.1 years. The steady lengthening of these time frames has been accompanied by improved controls, but it has also implied increased costs. Currently, the time it takes for a new molecule to become an approved drug is on average 12 to 15 years and requires a total investment of around 600 million dollars. Diverse professionals participate in this process, including organic chemists, molecular biologists, toxicologists, physicians,

pharmacologists, biomedical professionals, and computer scientists. One out of every ten molecules is developed, and only one out of every 5,000 drugs that makes it to clinical trials will end up having a therapeutic use.⁽⁵⁰⁾

Taking the global population as the target population for clinical trials would constitute a time-saving measure. Large numbers benefit everyone – both patients and the industry – and therefore the fundamental problem is reaching a level of compensation that corresponds with the real effort put forward by each researcher. However, spontaneous strategic alliances can bring about a number of difficulties, such as the loss of autonomy in decision making, the effort needed for coordination, the need to align interests, and increased organizational complexity. Technology sharing can be useful for a project, but that same technology may be used by competitors on other projects, creating difficulties with unifying diverse corporate cultures.

Lastly, improved synchronization between local agencies – such as the Food and Drug Administration (FDA), the European Medicines Agency (EMA) or the Japanese Ministry of Health – would reduce the amount of time needed for drugs to reach the market, which would in turn lower costs.

An analysis of the pharmaceutical companies with a presence in Spain reveals evidence of a relationship between the development of new products and the formation of strategic alliances.⁽⁵²⁾ In this regard, a major study looked at new products already on the market as well as those in clinical trials and analyzed their probabilities of reaching the market using the methodology proposed by Kellog and Charnes.⁽⁵²⁾ Nevertheless, this study did not reach the same conclusions with respect to the relationship between the number of patents and the development of new products and strategic alliances. This could be due to the fact that active substances are patented in the initial stages of biopharmaceutical research, but many do not constitute an innovation.

It is clear that not all alliances present the same results and many involve risks, but nonetheless the work of healthcare authorities

should attempt to improve collaboration models. Circumstances such as these necessitate the proactive participation of the public sector, armed with a number of formulas ranging from concrete alliances to pharmaceutical consortia. Companies will benefit from a clear definition of property rights, savings on clinical trials, and all of the other benefits associated with economies of scale, in addition to public sector support for research efforts. Drawbacks include the moral risk of possible disloyal behavior on the part of a partner and greater controls placed on research spending. Moreover, patent protection would be subject to the existing legal order, although public participation opens up possibilities for price reduction in developing countries.

DISCUSSION AND CONCLUSIONS

Given that patents are a valuable component of cost sustainability and disease reduction from an economic standpoint, investment in patents is viewed in a positive light. Patents are an investment that can be financed by the private sector, by the public sector, or through some type of mixed arrangement, and can be national or international in their reach. Additionally, they must have precise objectives, clearly defined distributions of costs and workload, and take into account the concept of epidemic or pandemic expansion as well as the longevity of pertinent modifications. All of this makes large volumes of financing necessary, which should be seen as an investment rather than a simple expenditure.

Previous studies⁽³¹⁾ have shown that in the health sector, increases in the number of patents paradoxically do not coincide with increased innovation. The sustainability of the health system is linked to healthcare coverage and spending efficiency. This has given way to the development of protective legislation with patent law, which has not been able to effectively stimulate innovation. Consistent with these findings, our study has identified the need for a mechanism to address market failures in efficiency and equity,

whereby the regulations of healthcare authorities foster a situation in which all involved parties are satisfied.

Regarding actions carried out in different countries to stimulate research and limit spending, it can be noted that patents have a minor presence in Central America, and therefore pharmaceutical innovation is dependent on third parties.⁽⁵³⁾

Furthermore, developing countries – with weaker invention capabilities in local pharmaceutical industries – are more prone to applying norms that favor competition rather than exclusiveness, as a tool for promoting access to health technology. However, when the invention capability in these contexts grows, new provisions will become necessary.⁽⁵⁴⁾

Certain limits exist with respect to patents regarding the stimulation of research. In times of a pandemic, solidarity-based courses of action can be observed internationally and throughout Europe, which generally attempt to make patents free of cost. This is aimed at facilitating licensing that will make possible the search for solutions such as “patent pools” and multilateral contract initiatives.⁽⁵⁵⁾ A further limit has to do with the application of the criterion of novelty, which indicates that patents are only granted for novel technologies; that is, that there has been restricted public access before it was patented.⁽⁵⁶⁾

Given the scientific relevance of the object of analysis considered in this study, we recommend supporting greater transparency regarding the production costs of pharmaceuticals, as well as strategies that will stimulate innovation, which will simultaneously ensure the sustainability of the health system. Similarly, we believe that it is both relevant and consistent with the findings of this study to further investigate the impact and effectiveness of biological treatments for rare diseases (or those with low prevalence) in order to determine their effects on sustainability, that is, what the system can and cannot bear.

A restructured economy would benefit from investment in the development of new products, strategic alliances, and tactics to lessen the impact of diseases or to forestall their expansion. Any economy would benefit

from patents, whatever its income level. It is clear that the challenges posed by infectious diseases that could potentially turn into pandemics demand two types of global actions: on one hand, international cooperation – in all of its forms, not just economic – and on the other, the solidarity implied by collective efforts, given that we are all exposed to the same threats, and if one country, region, or population group is left without coverage, that implies a risk for all others.

In the context of this study it should be noted that in recent decades, health improvements in developed countries have been possible due to research on the treatment of chronic diseases (cardiovascular, neurological, and in particular oncological). Mortality caused by infectious disease had become secondary, opening up debates over whether or not maintaining universal health systems with current levels of entitlements would be sustainable. These discussions were largely susceptible to ideological debates. In fact, after the 2008 crisis, Royal Decree-Law 16/2012 reduced coverage of undocumented immigrants, in an attempt to diminish spending on the treatment of chronic diseases by excluding certain groups. Nonetheless, globalization and the appearance of new diseases such as A-H1N1, SARS2, Covid-19 – or even Ebola, which made its way to Europe and the United States – have rendered these debates obsolete. One infected person can transmit the disease to dozens of others, regardless of their income level or medical coverage.

The pharmaceutical industry has managed to secure protection for research on new drugs through patent law, both in international agreements and domestic legislation. In some cases this has taken the form of questionable uses of patents, such as the practices known as blanketing, flooding, and fencing, as well as the strategy of secondary patenting, which seeks to extend the period of market exclusivity. New models of compensation for research on new drugs – such as value-based payment models, risk sharing, and improved administrative strategies in negotiation processes – represent alternative corporate financing models that can provide

incentives for innovation to a degree, despite not fully resolving the issue of patenting.

New health emergencies warrant new ways of thinking about the future. Public-private partnerships, the internationalization of clinical trials and research processes, and the creation of pharmaceutical research and marketing consortia all allow for economies of scale and time saving in both research and clinical trial phases.

Public sector participation should be oriented toward leading research priorities, with financial support that varies as a function of

private sector risk, as well as greater harmonization between agencies and health authorities responsible for the approval of drugs. It is a common occurrence that a drug is approved by one agency but then takes years to obtain approval from another, or is simply not approved; this was the case of Edaravone, a neurological drug that was approved both by the FDA and Japanese authorities, but never gained approval from the EMA. Unified criteria would provide greater security to patients and would significantly reduce costs.

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CITATION

Gómez Franco T, Matarín Rodríguez-Peral E, García García F. The sustainability of the health system and the pharmaceutical market: A permanent interaction between the cost of medications, the patent system, and disease care. *Salud Colectiva*. 2020;16:e2897. doi: 10.18294/sc.2020.2897.

Received: 7 Jun 2020 | Modified: 21 Aug 2020 | Accepted: 25 Aug 2020 | Publication online: 17 Oct 2020



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<https://doi.org/10.18294/sc.2020.2897>

This article was translated from Spanish by Joseph Palumbo