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Rationalizing Pharmaceutical Spending

Manuel García-Goñi

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Rationalizing Pharmaceutical Spending
Prepared by Manuel García-Goñi[†]

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ABSTRACT: Pharmaceutical spending accounts for a large share of health spending worldwide. While pharmaceuticals are an indispensable component of effective modern health systems, and their benefits in terms of increasing life expectancy and improving quality of life are unquestionable, the large variation in pharmaceutical spending across countries suggests that there may be large efficiency gains to be realized. This paper reviews the existing literature and databases on the level and composition of pharmaceutical spending and estimates potential efficiency gains from increased use of generics. It also reviews how countries organize the procurement and tendering of pharmaceuticals and the implications for spending. Finally, the paper identifies the various channels through which spending inefficiencies can arise and identifies reform options for reducing pharmaceutical spending while ensuring quality health outcomes.

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WORKING PAPERS

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Glossary

ATC	Anatomic Therapeutic Chemical
CEA	Cost-Effectiveness Analysis
DDD	Defined Daily Dose
EMA	European Medicines Agency
ERP	External Reference Pricing
EU	European Union
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
HTA	Health Technology Assessment
INAHTA	International Network of Agencies for Health Technology Assessment
INN	International Non-proprietary Names
IRP	Internal Reference Pricing
LMICs	Low-and Middle-Income Countries
MEA	Managed-Entry Agreements
NICE	The National Institute for Health and Care Excellence
OECD	Organization for Economic Co-operation and Development
PPP	Purchasing Power Parity
R&D	Research and Development
SDF	Specific Drug Funds
TRIPS	Trade-Related Aspects of Intellectual Property Rights
VBP	Value-Based Pricing
WHO	World Health Organization
WTO	World Trade Organization

I. Introduction

Pharmaceutical products are an indispensable component of effective modern health systems, and managing access is crucial for ensuring that people have the affordable, quality health care they need for healthy lives (Seiter, 2010; Kruk and others., 2018). They have a large positive social impact through contributing to the increase in life expectancy (Cutler and others, 2006; Lichtenberg 2014, 2016) improving quality of life of patients (Scherer, 2000; Lichtenberg and Virabhak, 2007), and reducing avoidable mortality or the presence of physical or cognitive limitations (Lichtenberg and Virabhak, 2007). Increased global access to essential medicines and other health products has saved, and improved the quality of, millions of lives (Center for Global Development, 2019). The use of new innovative pharmaceutical products has also changed the way healthcare is provided, e.g., facilitating a lower average length of stay at hospitals and increasing the relative role of outpatient ambulatory care (Lichtenberg, 2019).

Increasing spending on pharmaceuticals has been accompanied by a growing policy focus on how to contain these costs (Carone and others, 2012). The large variation in pharmaceutical policies and costs across countries suggests that there may be large efficiency gains to be realized. Many countries have implemented various policy measures aimed at promoting more cost-effective use of pharmaceuticals and value for money. The primary focus of this paper is to review the relevant literature on pharmaceutical spending and pharmaceutical policy, as well as the data available to inform the choice and design of key policy measures that can help increase the efficiency of pharmaceutical spending to enhance value for money and contain costs. The structure of the paper is as follows:

- Section 2 provides a brief overview of the basic economics of pharmaceuticals from both the supply and demand sides.
- Section 3 discusses the main international databases that contain information on the level and composition of pharmaceutical spending, the increasingly important role of pharmaceuticals in total health expenditures, and the overall architecture of health systems. We differentiate between outpatient pharmaceutical expenditure (prescribed and over-the-counter medicines) and expenditure on inpatients in hospitals given the increasing share of the latter in total pharmaceutical expenditures.
- Section 4 describes how the level and composition of pharmaceutical spending varies across countries and over time. It also identifies key information gaps that exist which limit the analysis of pharmaceutical spending efficiency and of possible reform options for enhancing efficiency.
- Section 5 reviews pharmaceutical policies being implemented in countries to enhance spending efficiency, including those directly related to the level of pharmaceutical expenditure (such as promotion of generics, reducing waste, centralized purchasing to secure lower prices, and use of co-payments).

- Section 6 focuses on procurement and tendering practices and the pros and cons of centralization based on country experiences.
- Section 7 discusses country reform experiences to draw lessons on which policies seem to work best in which circumstances.
- Section 8 provides a summary and concluding remarks.

II. The Economics of Pharmaceuticals

Total (public plus private) health expenditures in OECD countries have increased significantly over recent decades, from an average of 4.6 percent of GDP in 1970 to 8.8 percent by 2018 (OECD Health Data, 2019), and is projected to continue to rise over coming decades (Clements, Coady and Gupta, 2012; International Monetary Fund, 2020). The variation across countries is also large, ranging from 16.9 percent in the US to 4.2 percent in Turkey. As a consequence, there has been growing interest in understanding the main determinants of the level and growth of health spending. Newhouse (1992) found that about half of the increase in health expenditures was determined by technological change. More recently, Willemé and Dumont (2015) and Nghiem and Connelly (2017) obtain similar results. Innovation in pharmaceuticals is an important component of health technology, as healthcare innovation is often related to the development of new pharmaceuticals with therapeutic added value (Oriana and others, 2016). While these developments come with significant improvements in population health and welfare, they also come with higher costs associated with increased use of higher quality but more expensive pharmaceuticals.

The pharmaceutical industry is one of the world's most research-intensive industries (Scherer, 2000) and also one of the most regulated markets due to the prevalence of market power among suppliers. The field of health economics has studied the interaction between supply and demand to understand efficiency in a market in which there is a significant presence of uncertainty. On the supply side, the development of new innovative pharmaceutical products is a long and expensive process (Scott-Morton and Kyle, 2012) that, if successful, culminates in the entry of an original product to a market usually protected by a patent. The companies that have developed a product use market power and lack of substitutes to obtain profits and compensate for high research and development costs. Without such protection, incentives for innovation would be diluted.

When the patent is expired, regulation may promote competition in different ways, such as fostering the entry of lower price substitutes to avoid excessive pharmaceutical expenditure and improve access. There are two different types of lower-price substitutes for innovative pharmaceutical products: generics and biosimilars. Whether the substitute for a pharmaceutical product is a generic or a biosimilar depends on whether that product is chemical or biological. When the pharmaceutical product is chemical, the substitute is a generic, while when the pharmaceutical product is biological, the substitute is a biosimilar product. Because of the

difference in the compound of chemical and biological products, the degree of substitution of generics and biosimilars with respect to their innovative products is different. Generics are exact copies of drugs of chemical origin and therefore are perfect substitutes for branded chemical products. Although biosimilars are also substitutes for original biological products, because of the biological compound existing in these products, biosimilars are not considered to be identical but similar to the original products with respect to quality characteristics and biological activity. The safety and efficacy of biosimilar products is established based on an extensive comparability exercise with their original biological products (European Medical Agency, 2014). Although biosimilars are used both in retail and in hospitals, most are used in hospitals.

Many countries use Health Technology Assessment (HTA) and cost-effectiveness analysis (CEA) as a tool for assisting in health care decision making (Garber and Sculpher, 2012) with respect to access, pricing and reimbursement of innovative products. CEA compares different options and evaluates whether the incremental benefit in the clinical outcome warrants the incremental cost of an improved or better product. CEA may, for instance, include not only the benefits and costs of the alternative pharmaceutical treatments but also any other direct or indirect cost of health provision, such as a decrease in the length of inpatient stays, which is usually much more expensive than outpatient and home care. This is intended to promote the objective of value for money, trying to obtain the greatest clinical benefit per monetary unit spent.

Health economics has also extensively analyzed the demand for pharmaceuticals. It is important to note that in many countries the public sector (through its health systems) is the main purchaser thus introducing the potential for (countervailing) monopsony power in the pharmaceuticals market. In such an imperfect market, the way in which procurement is organized can determine the cost of the medicines, and hence their access for the population and the efficiency of pharmaceutical expenditure.

Procurement is even more relevant in low- and middle-income countries (LMICs), where sustainable and equitable access for all to essential medicines is key for a universal health coverage system focused on quality (Wirtz and others, 2017). As Seiter (2010) points out, access to medicines can be decomposed into four dimensions: accessibility (a person's ability to physically reach a health center or other outlet where drugs can be prescribed and sold), availability (availability of the adequate medicines at the place of service or the attached or contracted pharmacy shop), affordability (costs to the individual for the treatment including price to be paid, but also other costs such as transportation costs or the loss of income because of absence from work), and acceptability (both the prescriber and the patient perceive the selected medicine as adequate, safe, and effective).

With respect to the consumption of medicines, its use is efficient when a patient receives and takes the right medicine to treat the symptom or disease, in the right formulation and dose, at the right time, and for the right duration (Wirtz and others, 2017). Any deviations from those conditions come along with inefficiency in the use of medicines. At the individual level, the efficiency of pharmaceutical spending is also affected by the extent of

insurance (or the level of copayment)—the more insured an individual is, the lower their perceived cost and the greater the incentive to purchase, even above the efficient amount (i.e., where the marginal cost equals the marginal benefit). Manning and others (1987) highlighted the inefficiency behind this moral hazard problem based on the results of a randomized experiment. As a consequence, copayments need to be designed so as to provide incentives to reduce abuse in the consumption of pharmaceuticals, and thus reduce inefficiencies in demand, but without reducing the efficient consumption based on need.

In summary, the overall focus of economics as applied to the pharmaceutical market is to design regulations and institutions that provide the right incentives for the efficient development of innovative products and promote the right degree of competition for the supply of non-protected pharmaceuticals and the efficient prescription and consumption of pharmaceuticals. It is not about reducing pharmaceutical expenditures per se but rather aimed at reducing waste and inefficiencies in pharmaceutical demand and supply given the needs of the population and to cost-effectively enhance population health and welfare through ensuring broad access to quality health care.

III. International Databases and Their Uses

A. Public Databases

The OECD is the most important source of international databases regarding pharmaceutical use and expenditure (OECD, 2019). The OECD Health Statistics¹ is published yearly and is the most widely used public database for international comparison. It contains information from 45 countries starting in 1960, although not all indicators are available for all countries. For instance, regarding the pharmaceutical market, it contains indicators on the consumption in Defined Daily Dose (DDD) per Anatomic Therapeutic Chemical (ATC) Classification, sales of pharmaceutical products on the domestic market (total and by selected ATC groups), or the share of generics in this market (in DDD or in sales). These data allow an analysis of pharmaceutical expenditure per capita (prescribed and over-the-counter medicines) and expenditure on other medical non-durables (in US dollar purchasing power and as a proportion of health expenditure), and also the level of out-of-pocket expenditure per capita. This database is therefore very useful for analyzing trends in pharmaceutical use and expenditure at the retail level (although not hospital expenditure), including the development and diffusion of generics. By appropriately controlling for the health needs (e.g., incidence of health conditions and demographic variables), this information may be used to explain differences in the pattern of pharmaceutical expenditures and identify possible inefficiencies in pharmaceutical expenditure due to excessive use or absence of effective regulation.

Importantly, not all countries report homogeneous information and there are limitations in the use of these indicators. Most countries report information on consumption and sales at the retail level, and for drugs that are

¹ [OECD Health Statistics](#)

reimbursed by public insurance, but only a few countries report information regarding consumption in hospitals. As a consequence, there is still no dataset available to perform a cross-country data analysis on pharmaceutical spending for the inpatient sector at the international level. As this information becomes increasingly available, it could be very useful for analyzing different consumption paths of pharmaceuticals at hospitals and complement the analysis that can already be performed with respect to retail pharmaceutical expenditures. This is important because most of the high-tech, innovative and expensive drugs entering the market are only prescribed or initiated in hospitals as, for instance, in the case of anti-rejection drugs for transplant patients or medicines used in conjunction with chemotherapy (Connors, 2017).

Pharmaceutical expenditure is determined by the product of volume and prices, and it is instructive to look separately at both magnitudes. The price at which sales are accounted for depends on the country and it might be the wholesale price or the reimbursed price.² Since prices drop when generics access the market and are more widely promoted, available information can be used to analyze the evolution of the market share of generics. However, there is still very little public information regarding the consumption of biosimilars in some specific markets (OECD, 2019). Although both generics and biosimilars are present in both retail and hospital consumption, the impact of generics is clearly observed in the retail market while most of biosimilars that are currently in the pharmaceutical market are administered in hospitals. Thus, improving the availability of information regarding the evolution in the market share and prices of biosimilars (compared to their biological originators) is crucial for the analysis of the efficiency of pharmaceutical expenditures in hospitals.

Besides the OECD dataset, it is possible to obtain some further data on pharmaceutical expenditures for other countries through the Global Health Expenditure Database from the World Health Organization. Also, the European Price Information Database (EURIPID)³, which is the result of a non-profit cooperation between different countries (mostly from the European Union), contains information on the pricing and reimbursement of medicinal products across countries (based on publicly reimbursed expenditures). This dataset is not public but only available to specific nationally designated bodies of the collaborating countries and is potentially very useful for designing pricing and reimbursement policies, for example, regarding the design of managed entry agreements for new innovative pharmaceutical products using information on the level of prices in the other participating countries (Habl and Fischer, 2021).

B. Private Database

IQVIA (formerly Quintiles IMS) is a private company that compiles information regarding sales of pharmaceutical products from a representative sample of a very extensive global network of pharmacies, hospitals, payers, and associations. This private dataset tracks every product in hundreds of therapeutic

² Detailed information on the methodology followed per country and the limitations of the data provided can be found [here](#)

³ Information available [here](#)

classes, and provides estimated product volumes, trends and market share through retail and non-retail channels (Quintiles IMS Institute, 2016). This dataset is considered high quality and is used by commercial, governmental, and academic researchers (Espín and others, 2018) to analyze in detail the use and expenditure in pharmaceuticals by class, country and region. This information makes it possible to predict the future path of pharmaceutical expenditure and to compare the effectiveness of the variety of health policies that are implemented in different countries.

IV. Evolution of Pharmaceutical Expenditures and Their Components

A. Retail Pharmaceutical Spending

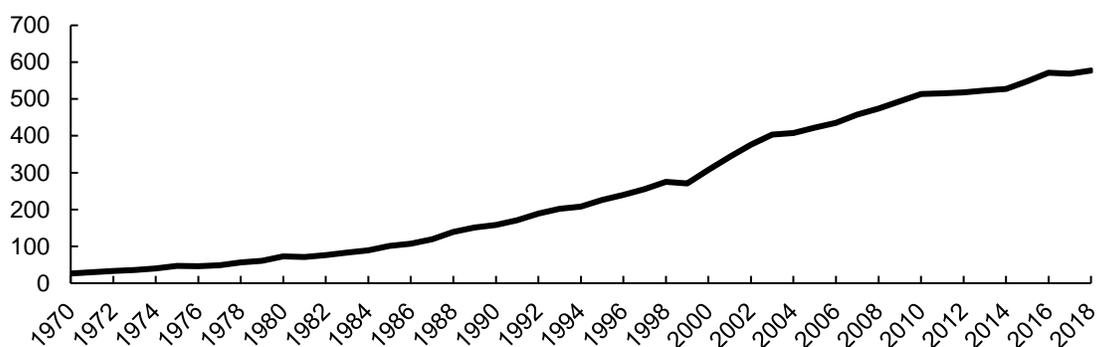
Most of the publicly available international data on pharmaceutical expenditures refer to sales at pharmacies through prescriptions and over-the-counter. Over recent decades, average per capita retail pharmaceutical expenditure (prescribed and over-the-counter medicines) in OECD countries has increased from 308 US dollars in 2000 to 554 US dollars in 2018 (Figure 1). However, there are significant differences in spending by country, from the highest expenditure of 1220 USD in the US (2017) to 251 USD in Mexico and 123 USD in Costa Rica (also in 2017) (OECD Health Data, 2019). On average, pharmaceutical (prescribed and over-the-counter medicines) expenditure constitutes 16.4 percent of total health expenditures, again with sizeable differences across countries (Figure 2). For instance, in Spain it was 18.6 percent and in Canada 16.7 percent, while it was of only 7.6 percent in The Netherlands and 11.9 percent in the UK.

The evolution of pharmaceutical expenditures is conditioned by the presence of generics in the market, depicted for a selection of OECD countries in Figures 3 (in value) and 4 (in volume). There is a marked increase in the market share of generics, in volume, while in value this increase is much more modest. The average of the 26 OECD countries reporting is a market share of generics of 24.9 percent in value and 52.4 percent in volume (OECD Health Data, 2019). Countries such as the UK, Germany, New Zealand and Turkey have relatively large market shares for generics, while Spain, Switzerland and France have low generic shares. Some countries opened their pharmaceutical markets to generics much earlier than others. By the year 2000, generics had more than 40 percent of market share (volume) in the UK, The Netherlands and Germany, while Spain, France and Switzerland only began entering the market at that time. The consistent increase in market share across countries reflects the impact of pharmaceutical policies promoting the entry and use of generics, such as the implementation of reference price systems or generic substitution at the pharmacy.

Moreover, the gap between the market share in countries using generics most intensively and those less intensively, especially in volume (figure 4), has not been significantly reduced, pointing to the great potential that still remains in many countries for decreasing pharmaceutical spending through expanding use of generics. A feasible explanation for this gap is the different level of success in the implementation of policies regulating

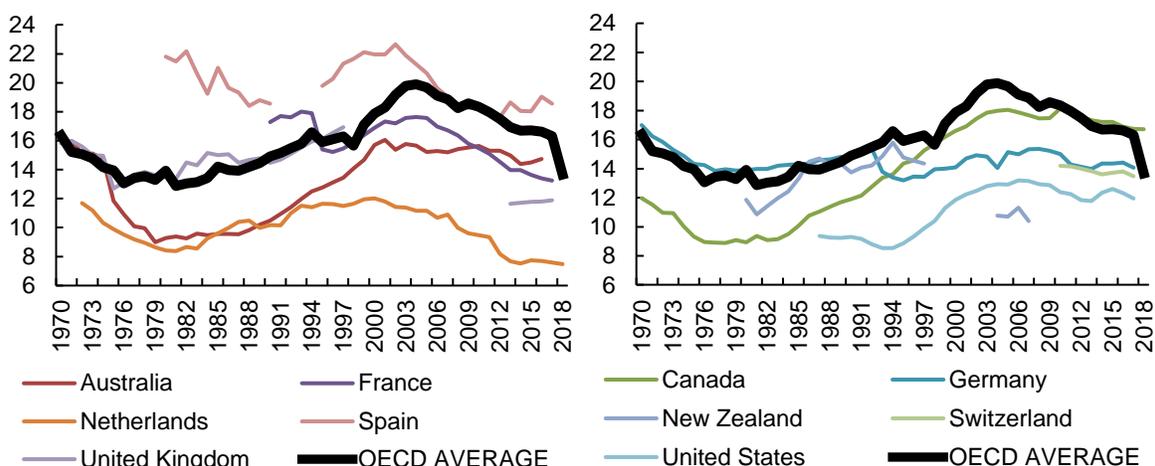
the choice of the drug by physicians and pharmacies. Puig-Junoy and Campillo-Artero (2019) point out that until 2006 countries such as Spain, Italy and France had a physician-driven pharmaceutical model in which most of the decision-making power in the choice of drug lay with the physician. Countries with high cost reductions, such as the Netherlands, the United Kingdom and the United States, have more pharmacy-driven models where the pharmacist has the power of choice by replacing a branded drug with a cheaper generic. In addition, Berndt and Dubois (2016) show that the introduction of generics in countries with pharmacy driven pharmaceutical models achieved a greater decrease in average prices.

Figure 1. Current Expenditure on Pharmaceuticals and Other Medical Non-durables
(OECD Average Current Per Capita, in US Dollar, PPP, 1970–2018)



Source: Data from the OECD Health Data (2019).

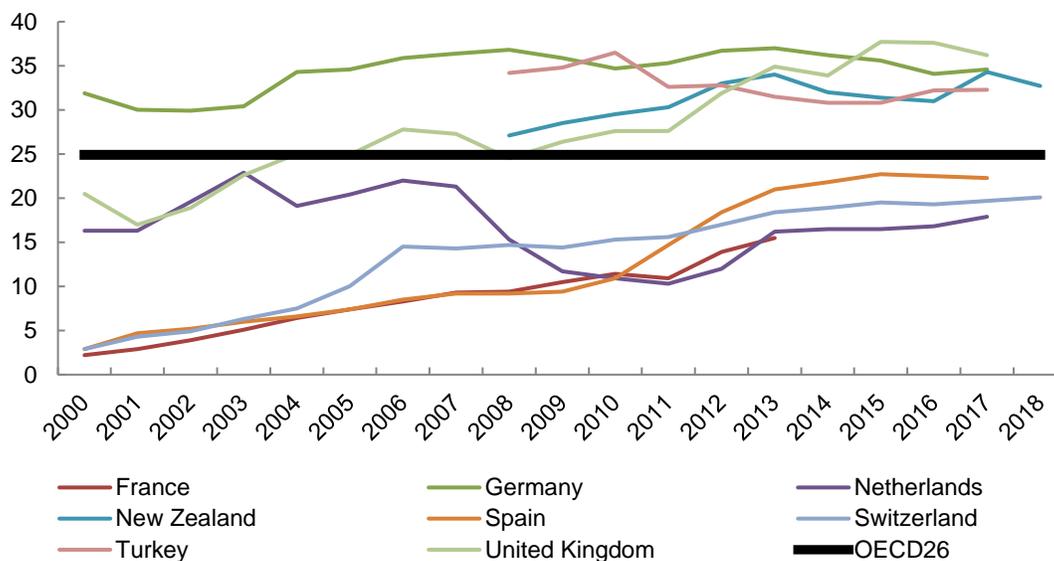
Figure 2. Share of Expenditures in Pharmaceuticals and Other Medical Non-durables



(Percent of Current Health Expenditure, 1970–2018)

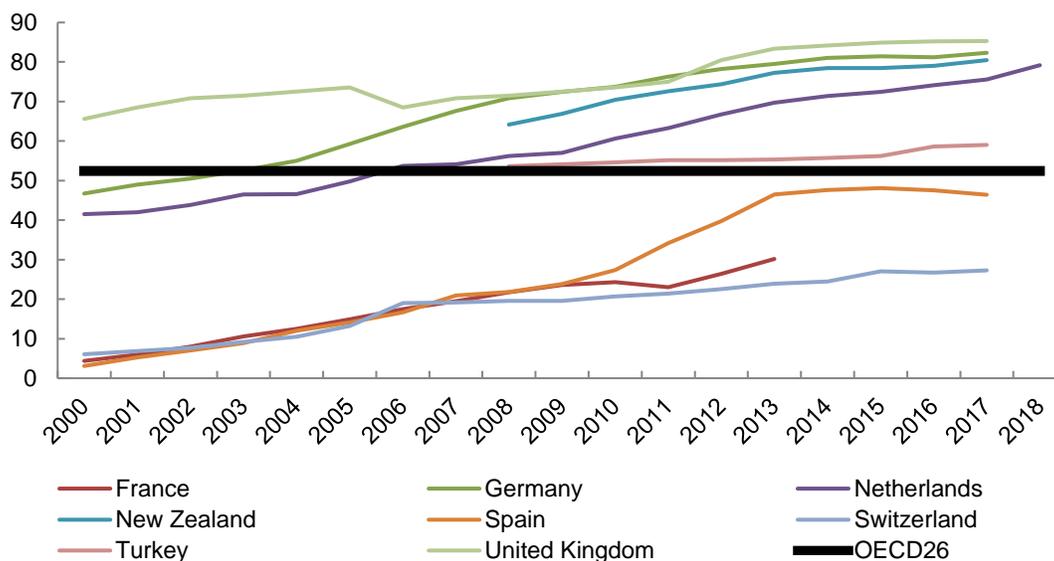
Source: Data from the OECD Health Data (2019).

Figure 3. Percentage Value Share of Generics in Reimbursed Pharmaceutical Market
(In Retail, Including the Average for 26 OECD Countries in 2017)



Source: Data from the OECD Health Data (2019).

Figure 4. Percentage Volume Share of Generics in the Reimbursed Pharmaceutical Market
(In Retail, Including the Average for 26 OECD Countries in 2017)



Source: Data from the OECD Health Data (2019).

To explore the relationship between the market share of generics and relevant variables regarding health and pharmaceutical spending, we performed regression analysis for the 18 countries for which OECD publishes this

information. Our five dependent variables were, in five separate regressions, pharmaceutical expenditures per capita, the share of pharmaceutical expenditures with respect to health expenditures, health expenditures per capita, the share of health expenditures with respect to GDP, and the share of pharmaceutical expenditures with respect to GDP. We used market share of generics as our independent variable, and we also controlled for country and year fixed effects and their level of GDP per capita. Table 1 shows the most relevant results and Annex Table A1.1 provides more detailed results. An increase of 10 percentage points in the market share of generics (in volume) is associated with a significant reduction in total pharmaceutical spending per person, resulting in an annual efficiency gain of 35.88 USD (PPP) per person and a reduction in total pharmaceutical spending as a share of GDP by 0.05 of a percentage point. These results suggest that the promotion of generics is associated with direct efficiency gains in pharmaceutical spending that releases resources to be allocated either to other health spending or to other sectors.⁴

**Table 1. Expected Change if Market Share of Generics
(in Volume) is Increased by 10 Percentage Points**

Pharmaceutical Expenditures per capita (PPP)	-35.88 USD
Share of Pharmaceutical Expenditures with respect to Health Expenditures	0.52%
Health Expenditures per capita (PPP)	-48.48 USD
Share of Health Expenditures with respect to GDP	-0.23%
Share of Pharmaceutical Expenditures with respect to GDP	-0.05%

Note: All coefficients are significant at 1% level.

Our model allows for a simulation of the efficiency gains that would be realized if the countries increased their market share of generics to higher levels achieved in other countries. We simulate an increase in the market share of generics up to the 75th percentile (70.05 percent) for all countries below these levels relative to the existing market shares (Annex Table A1.2). We present our results for year 2017, as the most recent year with data available for most countries. The UK, Germany, New Zealand and The Netherlands have volume market shares for generics equal to or greater than the 75th percentile, and therefore we do not simulate savings for

⁴ We also find that increasing the market share of generics by 10 percentage points is associated with increases of the share of pharmaceutical expenditures in total health spending by 0.52 of a percentage point, and with reductions of total health spending as a share of GDP by 0.23 of a percentage point, although there is no significant changes associated in the level of annual total health spending per capita.

these countries. France is also out of our results because it has not reported the market share of generics in retail since 2013, while Turkey is only partially present due to lack of data.

Potential savings and efficiency gains will be greatest for countries with lower market shares of generics. Annex Figure A1.1 shows annual current pharmaceutical spending per person and that estimated with our model if the market share of generics goes up to the 75th percentile. The difference represents potential savings (Table A1.2), which are greater than 15 percent in countries such as Belgium (17.06 percent), Greece (25.74 percent), Ireland (18 percent), Italy (26.67 percent), Luxemburg (37.92 percent), Portugal (15.36 percent), and Switzerland (15.93 percent). At the same time, our simulation quantifies a decrease in the share of GDP devoted to pharmaceutical spending (Table 2 and Appendix Table A1.2) greater than 0.10 percent of the GDP in most countries, such as Belgium (0.16 percent), Greece (0.21 percent), Ireland (0.15 percent), Italy (0.22 percent), Luxemburg (0.29 percent), Spain (0.12 percent), and Switzerland (0.21 percent). Countries such as Austria, Denmark and Slovak Republic present lower savings in terms of current pharmaceutical spending or share of the GDP because their current share of generics is closer to the level in the 75th percentile. At the same time, countries like Luxemburg, Italy, Greece or Switzerland present the greatest level of savings in current annual pharmaceutical spending per person (211, 157, 155 and 153 USD PPP respectively) because they present the lowest share of generics in the pharmaceutical market (retail).⁵

Table 2. Estimated Annual Efficiency Gains when Market Share of Generics Increased to 75th Percentile

Country	Pharmaceutical Spending (per person, in USD, PPP)	Pharmaceutical Spending (per person, in percentage)	Decline in the share of GDP devoted to Pharmaceutical Spending (in percentage)	Health Spending (per person, in USD, PPP)	Decline in the share of GDP devoted to Health Spending (in percentage)
Austria	55	8.47	0.07	74	0.35
Belgium	118	17.06	0.16	159	0.76
Denmark	25	7.73	0.03	33	0.16
Greece	155	25.74	0.21	210	1.00
Ireland	108	18.00	0.15	146	0.69
Italy	157	26.67	0.22	213	1.01
Luxembourg	211	37.92	0.29	285	1.36
Portugal	62	15.36	0.08	84	0.40
Slovak Rep.	20	3.45	0.03	27	0.13
Spain	85	14.19	0.12	115	0.55
Switzerland	153	15.93	0.21	207	0.99
Turkey	40	-	-	54	0.26

Source: Authors' calculations.

⁵ Our simulations also show an increase in the share of health expenditures devoted to pharmaceuticals, savings in the share of GDP devoted to health, and no significant change in the level of annual health spending per capita (Table 2 and Appendix Figures A3 to A5). While the estimated potential gains from the expanded use of generics are substantial, realizing them could be difficult and requires strong political will and social support.

B. Pharmaceutical Expenditure in Hospitals

The growth rate of pharmaceutical expenditures in hospitals for a selection of OECD countries reporting this information is greater than that of retail pharmaceuticals (Figure 5). As a consequence, it is increasingly important to take into account pharmaceutical expenditure in hospitals when analyzing total pharmaceutical expenditures since this accounts, on average, for an additional 20 percent on top of retail spending (OECD, 2019). Among the reported countries, only Canada and Israel present a relatively greater growth of pharmaceuticals retail expenditures, while in Greece (with a strong policy to reduce wasteful use of drugs and of general budgetary cuts) spending on pharmaceuticals has decreased substantially both in retail and hospitals. In Czech Republic, Germany, Korea and Spain, there is positive growth of pharmaceutical expenditures both in retail and hospitals, the latter being significantly greater. Interestingly, countries like Denmark, Finland, Iceland and Portugal, have decreased expenditure on retail pharmaceuticals but have increased expenditures on pharmaceuticals in hospitals.

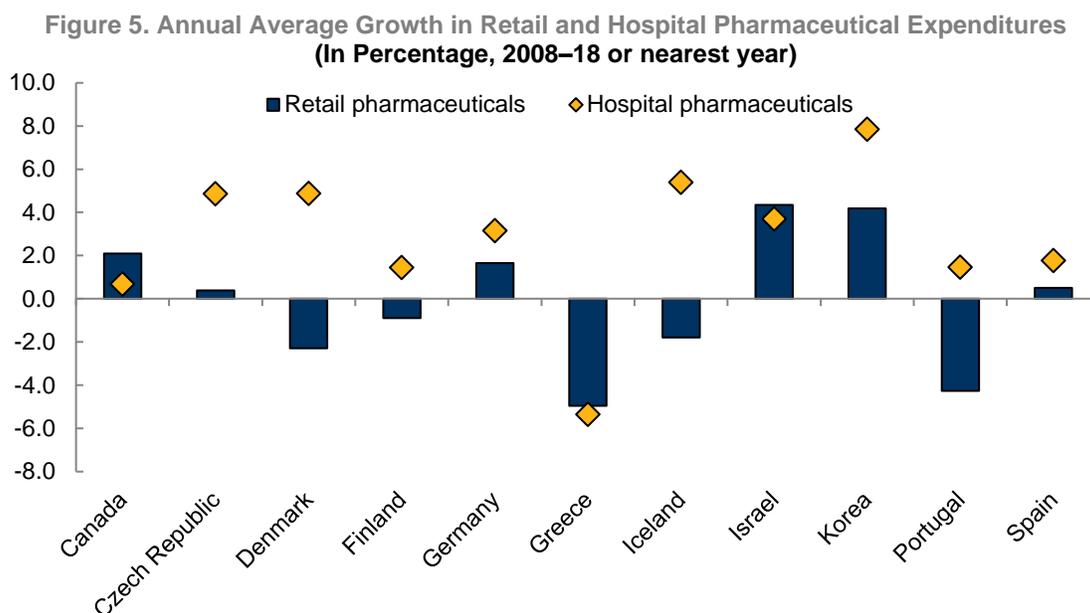
In general, the greater growth in pharmaceutical expenditure in retail compared to in hospitals in some countries, and the negative evolution of prices, may be explained at least partially by the implementation during the 2000s of pro-competitive policies in favor of generics. These policies include the introduction of internal reference price systems, generic substitution in prescriptions, and cuts in pharmaceutical prices that took place during the economic crisis (especially in Spain and Portugal) and in France, Germany and Ireland (Deloitte, 2013).

In contrast, expenditures on pharmaceuticals in hospitals are more affected by the entry of innovative products with high prices over the last decade, such as the increase in innovative oncology treatments or hepatitis C drugs. The process of setting prices for new pharmaceuticals varies across different health systems and countries at different income levels. Countries with a greater focus on value-based medicine may allow for higher prices while countries using external reference pricing systems and with lower income levels may be more focused on controlling the listed price of the medicine, although listed price often do not reflect net prices of medicines when there are discounts (Espín and others, 2018).

Procurement is especially important in the case of pharmaceuticals in hospitals because, in a fragmented health care system, decisions made at the hospital level may reduce the market power of the rest of the health system in bargaining over prices. Hence, the financing model and the architecture of the health system may be a factor explaining the different evolution of pharmaceutical expenditures. In general, all methods of paying providers (capitation, fee for service, salaries or pay for performance) have advantages and disadvantages. However, it is necessary to encourage quality and efficiency, including tackling waste and corruption, cost-effective medicine selection, and an appropriate procurement strategy (World Health Organization, 2010).

Hence, while retail pharmaceutical expenditure grew at a lower rate, or even declined, since the financial crisis, hospital pharmaceutical spending has tended to expand in a number of countries and has become a major

concern (Belloni and others, 2016), and most of the expensive technologies which tend to be the biggest cost drivers, are intended for hospital administration.



Source: Figure 10.3 in OECD Health Statistics 2019.

V. Cost-containment policies in pharmaceuticals

The growth of pharmaceutical expenditure can be decomposed into changes in prices, changes in quantities, and changes in the therapeutic mix used (Belloni and others, 2016). Many countries have implemented a number of cost-containment policies, some focusing on the supply side of pharmaceuticals (controlling their price and the combination of products in the market, including innovative products) while others focus on the demand side (avoiding excessive consumption). The discussion below focuses on key policies aimed at enhancing spending efficiency including: reducing medicine waste, adoption of an external reference price system for setting purchase prices based on those achieved in other countries, promotion of generics (in markets without protected chemical products) and of biosimilars (in markets where the patent of a biological originator product has expired), the pricing and entry of innovative products in protected markets, and demand-side policies such as copayments.

A. Medicine Waste

Efficient health spending requires that medicines are appropriately prescribed by physicians based on clinical guidelines and used by patients as prescribed. Wasteful clinical care refers to the provision of health services

that fail to maximize health outcomes with the available resources for reasons that could be avoided (OECD, 2017). Such waste could manifest itself through the existence of preventable adverse events that could be avoided through a better combination of health services, or low-value care that is ineffective, inappropriate and thus not cost effective. Fewer than half of all patients treated in low- and middle-income countries (LMICs) receive primary care according to clinical guidelines for common diseases, and half of all medicines globally are inappropriately prescribed, dispensed, sold or used (World Health Organization, 2009, 2010).

Inefficient use of medicines can be a consequence of incorrect diagnoses that may result in deleterious consequences for health (Kruk and others, 2018), such as treatment delays that in the case of patients with life-threatening emergencies may substantially increase mortality risk (Kruk and others, 2018), or the over prescription of antimicrobial therapy thus strengthening antimicrobial resistance (Mendelson and Matsoso, 2015). Other causes of inefficient use of medicines are underuse of effective care (Glasziou and others, 2017) or the overuse of unnecessary or ineffective care (Brownlee and others, 2017; Li and others, 2015) which is prevalent in LMICs (Kruk and others, 2018). Even after being diagnosed, many patients with HIV (Levi and others, 2016), tuberculosis (Subbaraman and others, 2016), diabetes (Manne-Goehler and others, 2016) or depression (Thorncroft and others, 2017) are untreated or undertreated in LMICs.

Effective educational programs and communications for patients on how to self-manage their health conditions or the importance of adherence to prescribed treatment have proved to be effective at avoiding the future need for health care and pharmaceutical expenditure. Also, direct communication between health professionals and patients before starting a new treatment has been proved to reduce wastage of medicine by up to 30 percent (OECD, 2017).

B. External Reference Price System

External (or international) reference pricing (ERP) is widely used in countries across Europe, Latin America, Southeast Asia, the Middle East or North Africa. The World Health Organization (2015) defines ERP as “the practice of using the price of a pharmaceutical product (generally ex-manufacturer price or other common point within the distribution chain) in one or several countries to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country”. The objective of ERP is to link the price of new drugs in the regulating country to the price of the same drug in a specified set of reference countries. Its application varies across countries (Kanavos and others, 2017), including the size of the country reference basket used, the type of country used in the basket, or the method of price calculation (Gill and others, 2019). Ideally, countries to be included in the basket should include those economically comparable and geographically close (Carone and others, 2012).

However, the use of ERP is not problem free. One concern is that the use of ERP could lead high-income countries to demand low prices enjoyed by the lower-income countries, which would create difficulties for the

latter. While, in the short term, the use of ERP in high-income countries might lead to lower prices, in the long run, a systematic lowering of prices would reduce revenues in the pharmaceutical industry thus diluting incentives for R&D investment and possibly the pace of innovation of new medicines (Danzon and Towse, 2003; Gill and others, 2019). This, in turn, could lead to higher prices in low-income countries and lower access to innovative medicines. As a result, ERP as a tool for controlling prices would appear to be more justified for countries with limited technical capacity or with difficulties in implementing price regulation mechanisms such as pharmaco-economic analysis (Espín, Rovira and Olry de Labry, 2011). The use of ERP in a country can also have cross-border spill over effects, such as price instability or strategic behavior by manufacturers through delaying access of new drugs in low-price (and low-income) countries to avoid lower prices in higher income countries (Vogler and others, 2019). Therefore, it is often argued that high-income or high-capacity countries should rely on more sophisticated pricing strategies using economic evaluation and cost-effectiveness analysis, while other should rely on ERP applied to economically comparable and geographically close countries.

It is important to note some obstacles associated with the implementation of ERP. For instance, it can be difficult to identify and compare prices against comparator countries due to differences in dosage, packaging, and even differences in the instructions or use reflecting clinical guidelines for the same molecule in countries in the basket. At the same time, there may be differences in reported prices (retail vs. ex-factory, wholesale) by companies, and it pressure from domestic producers to promote domestic production is frequent. Persson and Jönsson (2016) argue that the use of ERP might lead payers and manufacturers to engage in different agreements including price–volume negotiations or confidential discounts to avoid the effect of lowering prices in other countries using ERP. By avoiding the impact via the ERP system, this effectively facilitates manufacturer price discrimination by country. They advocate a pricing system in which there is price discrimination across countries and an increasing role for value-based pricing.

Box 1. 14 Best Practice Principles for Benchmarking in an ERP System

I. Objectives and scope of external price referencing system

1. ERP system objectives should be clear and align with country-specific health system objectives.
2. ERP systems should focus on in-patent products considered for the purposes of coverage, pricing, and reimbursement decisions.
3. Prices developed using ERP should not override conclusions of HTA or VBP approaches.

II. Administration and operations

4. The ERP system should have administrative simplicity and transparency
5. Stakeholders should participate in the design and review of the ERP system
6. Stakeholders should be able to appeal regulator decisions
7. Reference countries should be selected based on similarities in economic status and health system objectives

8. International implications of ERP implementation should be considered

III. Methods for the conduct of external price referencing

9. Publicly available ex-factory prices should form the basis of the ERP system
10. The mean of prices in reference countries should be used
11. Patent status should be respected
12. ERP formula should avoid the impact of exchange rate volatility

IV. Implementation of external price referencing

13. Price revisions should be kept to a minimum and should be carried out consistently to avoid the perception of opportunistic behavior
14. ERP- based prices should be aligned with other tools used when negotiating reimbursement

Source: Box 1 in Gill and others (2019).

If used, the ERP system should be transparent, simple, stable and sustainable, and designed to benefit all stakeholders, improve the accountability of decision making, reduce uncertainty for the pharmaceutical industry, and lower the risk of discrimination and corruption (Gill and others, 2019). Given its widespread use, recent papers in the literature have reviewed the international experience with the use of ERP (Gill and others, 2019; Kanavos and others, 2017; Belloni and others, 2016; Vogler and others 2019; Fontrier and others, 2019). Gill and others (2019) provide 14 best-practice principles for benchmarking using the ERP system (Box 1). Vogler and others (2019) recommend regular evaluations of prices to bring down prices and avoid delay in the entry of innovative pharmaceuticals through the strategic behavior of manufacturers.

C. Promotion of Generics

Once the patent of a pharmaceutical product is expired in a country, there is the possibility to increase competition and hence to reduce prices and pharmaceutical expenditures for that drug through the entry to the market of other products. When the original medicine is a chemical product, the generic is an exact copy and hence a perfect substitute. Generic drugs are bioequivalent replicas of brand-name drugs, containing the same active ingredients and with identical quality, safety, and efficacy profiles (Davit and others, 2009). The differences between generics and their originators are limited to inactive ingredients, like coloring, flavoring, and stabilizing agents, and their price is lower because it is cheaper to bring them to a market that already exists (Wouters and others, 2017). The World Health Organization (WHO) defines generics as multi-source pharmaceutical products that are therapeutically equivalent and interchangeable, not taking into consideration whether or not the 'originator' molecule is, or was, under patent protection (Belloni and others, 2016).

By obtaining the same clinical benefit at a lower cost, generics are an ideal candidate to contain pharmaceutical expenditures and many countries have implemented policies promoting their use. Belloni and

others (2016), World Health Organization (2015) and Kaplan and others (2016), among others, have reviewed such policies. Most studies focus on their impact on the supply side.

First are those policies related to the speed at which generic products are approved once the patent is expired, and the provision of incentives to generic manufacturers to file an application for market authorization. In some countries, the promotion of early access is executed through a license to develop a generic version of an originator product still under patent (research exemption in the US or Bolar provision in Canada). In addition, there are other policies that address the impact of free trade agreements on access to generics medicines, especially for LMICs, or other intellectual property rights granting some market protection to the first generic manufacturer entering the market so that there are greater incentives to arrive the earliest. The quality of generics is also strongly regulated, especially with regard to safety and efficacy and the equivalence to the originator product, in some cases expediting the review period for the access of the generic relative to the original product.

A second set of policies is intended to increase the degree of competition in the market. These include the promotion of entry of a sufficient number of manufacturers of generic products or the entry of therapeutic substitute products (Kaplan and others, 2016).

With respect to pricing, countries often implement policies to control prices in the market, such as setting prices for generics relative to prices of originator products or via internal reference pricing (IRP). IRP is a pricing policy that establishes a reimbursement level or reference price for a group of interchangeable medicines (Dylst and others, 2012). It is also possible to establish some control over the originator price, which can indirectly have some impact on the prices of generic products through the previously mentioned ERP or with value-based pricing (Kaplan and others, 2016). Cost-plus pricing strategies are also used, especially in LMICs, by setting a price to cover the cost of production, R&D and some other activities such as promotional expenses. In high-income countries the use of auction or tendering systems is common (Kaplan and others, 2016) as are price cuts (Belloni and others, 2016). Enhancing transparency on prices is also considered a key policy to foster effective competition in the market (World Health Organization, 2015; Kaplan and others, 2016).

Some other policies that are implemented are worth mentioning. Spain is the only country in the EU with a target price, which excludes coverage or public financing of the product if its price is above a reference price set for products within a homogeneous group. In fact, in the Spanish model there is no freedom for the price to differ from the reference price nor is there the possibility for the patient to choose a more expensive medicine at a higher co-payment (Puig-Junoy and Campillo-Artero, 2019). This policy punishes generics because it dilutes the only advantage of the generic, which is a lower price. Under this policy, brands are generally set at the reference price. This might partially explain the recent slowdown in the market of generics and the reduction in sales of active ingredients that have recently lost patent protection (Puig-Junoy and Campillo-Artero, 2019).

Another set of policies is aimed at mandating use of generics or influencing consumption towards generics. These include: preferential procurement of generics (usually reimbursed by the national health systems), promoting or making it mandatory to prescribe generic products (France, Greece, Hungary, and Japan) or to prescribe using International Non-proprietary Names (INN) (Estonia, Portugal, Spain, and France), and promoting or making it mandatory for pharmacists to substitute branded products and dispense generics at the pharmacies (Belgium, France, Ireland or Japan). However, it is important to note that there is generally significant resistance among policy makers towards policies that promote generic prescription and dispensing, stemming from political unpopularity and public pressure in favor of brand names. In order to overcome this obstacle, well-planned educational programs and media campaigns targeted at broader population, but also at physicians and pharmacists, must accompany such policy decisions to support successful implementation. Examples of education programs for the population to encourage consumers to buy generics can be found in Austria, Estonia, France, Island, Ireland, Luxemburg, Portugal or Spain (Belloni and others, 2016; World Health Organization, 2015; Kaplan, 2016).

The most commonly used generic promotion policies in the OECD since 2008 that have resulted in lowered prices are the mandatory prescription using INNs, incentives for doctors to prescribe generics, incentives for pharmacies to dispense generics and pressure on prices through auctions and price cuts (Belloni and others, 2016). As mentioned above, the weight in the choice of drugs between physicians and pharmacies also matters, and policies promoting generics are more successful in lowering prices in countries where pharmacists have a more important role (Puig-Junoy and Campillo-Artero, 2019; Berndt and Dubois, 2016). Where such policies are not yet in place, priority should be given to convincing physicians, pharmacists, and patients that generic drugs are bioequivalent to branded products and requiring generic prescribing and substitution (Wouters and others, 2017).

At the same time, in many countries, but especially LMICs, there is ineffective implementation or enforcement of existing policies which could be addressed through a combination of different approaches directed at different levels of the health system, such as INN prescribing, generic substitution, regulatory measures, financial incentives, sanctions, information provision, or better monitoring systems (Kaplan and others, 2016). It is also important to look carefully at the intellectual property provisions as these can lower the price of generics in the short run, although the decrease may not be substantial if they do not generate competition and there is need for monitoring to ensure that they improve the ultimate goal of accessibility (Kaplan and others, 2016).

D. Pricing and Entry of Innovative Products

New medicines may be new chemical entities or new formulations of existing drugs, ideally improving the treatment options for patients with specific conditions. New formulations can potentially reduce cost through fostering competition. However, new innovative drugs that improve therapeutic treatments and provide better quality care or address unmet needs for patients often change the combination of therapeutic products that are

used in the market (Belloni and others, 2016), are protected by patents, and typically involve a price greater than that of the existing alternative. Hence, they tend to increase pharmaceutical expenditures. Where feasible, economic evaluation or cost-effectiveness analysis (pharmacoeconomics) should be used in setting prices for innovative products.

Although there is no universally agreed definition of innovation for HTA agencies, it seems clear that innovation refers to new methods, ideas or products which are claimed to offer benefits over existing ones, and thus are generally patented products (pharmaceuticals and devices) with marketing authorisations. However, other relevant sources of innovation would be new ways to deliver services as well as new surgical, diagnostic and other procedures (Claxton and others, 2009).

Health Technology Assessment (HTA) is “a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system”⁶ (International Network of Agencies for Health Technology Assessment). In practical terms, the use of HTA means that reimbursement may be conditional on meeting specific clinical and/or economic cost-effectiveness criteria (Carone and others, 2012). In Europe, HTA is used: to inform reimbursement and/or pricing decisions (France, Italy, the Czech Republic or Switzerland), to reimburse a new product (with or without restrictions), to reject funding (in England, Sweden and Norway), or to decide about pricing and reimbursement when the new medicine presents uncertainty on clinical benefits or budget impact (Vogler and others, 2017). As pointed out by Davis (2014), taking into account that there may be costs associated with delivering the technology besides its price (e.g., by varying other aspects of resource use), even a zero-priced technology might be considered too not be cost-effective.

The use of HTA and economic evaluation can inform **Value-based Pricing (VBP)**, which relates the price of the innovative medicine to its added therapeutic value through comparison with existing treatments and can help set a price according to the ‘value’ the drug brings to the health system. This approach can provide the right incentives for investing in research and development to develop medicines with high value. However, HTA appears to be a superior strategy for obtaining value for money (Drummond and others, 2011). VBP is difficult to implement, especially in therapeutic areas where no alternative treatment is available and patients suffer from severe life-threatening disease, such as oncology or rare diseases. Furthermore, many LMICs do not have the adequate capacity to perform and properly use HTA. In such cases, the value of such products may not be easily reduced to clinical benefits and there is often strong public pressure that leads the authorities to pay high prices for limited clinical benefits (Vogler and others, 2017). As a result, it is not an easy task to set a price using VBP for many innovative drugs. Another limitation of VBP is that it presents opportunities for strategic behavior by the manufacturer in the economic evaluation exercise, especially when there is a unique price for a product that can be used in different markets (or as a second- or third- line therapy in the same

⁶ [International Network of Agencies for Health Technology Assessment \(INAHTA\)](#).

market) but where there is different added value in each market. In such cases, the manufacturer could seek to maximize profits by seeking entry to the market that ensures a better price for all other uses of the product. Finally, discussions between the health authority and the manufacturer regarding their different perceptions of value can be time and resource intensive (Kanavos and others, 2010). Another obstacle for the implementation of VBP is the discrepancy between the price charged and how much health systems can afford to pay for the benefits they offer (Claxton, 2016).

An alternative for setting prices for innovative pharmaceutical products is through **Managed-Entry Agreements (MEA)**. MEAs are agreements between the payer and the manufacturer that can vary in complexity. This may involve simple discounts and price–volume agreements in a financial-based scheme, without being related to clinical outcomes. Or it can be related to clinical outcomes, such as performance-based schemes that establish a direct relationship between the final price and the observed health outcome (Vogler and others, 2017). The existence of MEA agreements may be confidential, as in France or Spain, or public, as in Scotland, England and Belgium, but ultimately the final discount is unknown. The advantage of MEA is that it provides a feasible early access of the innovative drug to the market, although without changing listed prices (the ones used for ERP) it may lead to price discrimination. Although MEAs are often used in Europe, there is still little evidence about their effectiveness in improving affordability and access (Vogler and others, 2017). However, there are also obstacles to the implementation to MEA. Legislative background including procurement legislation needs to be provided for such agreements, which by their nature are typically confidential and not publicly available. Also, it is necessary to build and develop a technical capacity among respective government bodies to effectively negotiate and develop contracts, as well as overcome any reluctance to negotiate with the industry.

Specific Drug Funds (SDF) such as Cancer Drug Fund have also been used to promote the early access to patients of innovative products. They usually are implemented with a specific budget to be used to ease the publicly financed access of those specific drugs to the market. The use of SDF is not exempt of problems: experience from the Cancer Drug Fund by the NICE in the UK teaches that the budget set tends to increase in time, which is not a sustainable solution (Claxton, 2016). Also, through the use of SDF, innovative medicines can be approved earlier and with less information and more uncertainty than they would in the case of HTA, allowing the collection of data to reduce uncertainty in a period of two years after commercialization. Although, in principle, accelerating access is a good feature, if the drug should be rejected based on HTA after receiving the post-access information this can create difficulties for more heavily used drugs. At the same time, its use makes the comparison exercise that is needed for economic evaluation more difficult (Claxton, 2016). One recommendation to improve the use of SDF is to implement the ‘only in research’ approach which would restrict the financed use of the drug to research that can resolve uncertainties, e.g., using randomised trials. That way it would be easier to consider whether the drug should be approved for widespread use or rejected (Claxton, 2016).

In order to provide the right incentives for producers, Claxon (2016) proposes to link the appraisal of the costs and benefits of new drugs with national rebate agreements, so that the rebates reflect the discrepancy between the prices manufacturers wish to charge for their products and how much the health system can afford to pay for the benefits they provide.

Importantly, the methodology used to set prices for innovative products needs to find prices that are low enough to guarantee an early entry to the market and access for patients to innovative drugs, yet high enough to promote incentives for further R&D to obtain better drugs in the future. It is therefore important to account for the R&D expenses. Wouters and others (2020) estimates the mean cost of developing a new drug in the range \$314 million to \$2.8 billion. At the same time, it may be convenient to orientate research and development activities so as to ensure that missing essential medicines are developed and made affordable for all. To that end, Wirtz and others (2017) suggest creating an Essential Medicines Patent Pool.

E. Cost-sharing

Cost-sharing involves requiring patients to pay for a proportion of the price of the medicine they consume (co-payment). Based on a randomized experiment, Manning and others (1987) examined how copayments (and the degree of coverage in the health insurance) affected consumption, finding that increasing copayments leads to a lower quantity consumed. However, the primary aim of copayment is not to reduce consumption per se but to reduce inefficient consumption by patients over the efficient amount where marginal cost of production is equal to the marginal benefit of consumption. Copayments are more likely to be effective for medicines demonstrating elastic demand since a relatively small variation in price will lead to a significant decrease in the quantity demanded, thus minimizing any adverse impact on economic welfare and access to valuable medicines.

Most countries implementing copayments use a low level of copayment, especially for patients in need, in order to avoid any reduction in the level of adherence to treatments. Copayments may also differ by the type of drug or according to its intended use (Portugal, Greece, Sweden, Iceland and Slovakia), by socio-economic status (income or employment status), or by age (among others, Spain, Italy and Turkey). It could consist of a fixed amount per prescription (England) or a percentage of the price, and some countries use a maximum out-of-pocket limit for the patient (Australia, Finland, Japan, and Germany) (Barnieh and others, 2014).

The implementation of copayments therefore needs to be designed with caution, especially when it affects low-income groups, as in the case of Medicaid beneficiaries in the US (Wallace and others, 2008) or in LMICs. Copayments may just lead to a shift from public to private expenditure or towards cheaper but less appropriate pharmaceutical treatments for the patient's clinical condition, maintaining inefficient consumption levels (Belloni and others, 2016). Or they may reduce adherence to prescribed treatments with higher costs related to worsening health incurred at a later date (Morgan and Lee, 2017).

VI. Procurement of Pharmaceuticals

Procurement systems have a crucial role to play in ensuring cost-effective access to medicines, as well as to other health inputs such as diagnostics, devices, and equipment (OECD, 2017; Center for Global Development, 2019). Although procurement is only one element of a functioning supply chain, it should be judged by its ability to deliver drugs to patients when and where they are needed (Seiter, 2010). A very common method of procurement of medicines is through tendering. Pharmaceutical tendering consists of bulk purchase of medicines by a central buyer at fixed prices over specific periods following a confidential bidding process (Wouters and others, 2017). It is designed to ensure the availability of the needed pharmaceuticals, in the required quantities, at reasonable prices and at a recognized quality standard (Kanavos and others, 2009). The goal is to use the monopsony power of the buyer, usually the public sector, to reduce prices by centralizing purchase for a larger population group. For that reason, tendering is considered as a form of strategic purchasing (Vogler and others, 2018). However, while the use of tendering is associated with lower prices and cost containment, its use is not devoid of problems and may result in shortage and supply disruptions (Dranitsaris and others, 2017; Heiskanen and others, 2017), especially in environments burdened with corruption which have previously enjoyed the advantages of a decentralized system, related to the complexity of the implementation of centralized procurement or to the reluctance to change. Another unintended consequence of tendering that has been observed is that it can result in a low degree of competition in the market with a small number of manufacturers (Danzon, 2014).

Seiter (2010) provides a list of the most typical problems in pharmaceutical procurement and their consequences, among which are the existence of corruption that might derive from drug shortages or quality problems that might go unsanctioned. Other important problems for the implementation of efficient procurement are the lack of motivation and training in the personnel taking decisions, the fact that the planning of amounts to be procured is based on past consumption only or on low-quality data, the lack of information about prices, the lack of capacity in the assessment of bids, or the existence of political pressure to buy from local suppliers.

A. Developed Economies

Tendering is viewed as an important policy tool for purchasing pharmaceuticals in many developed economies, with numerous studies of this practice in European countries. Tendering is important for the procurement of both generic and non-generic pharmaceutical products and of both retail and hospital pharmaceuticals (Kaplan and others, 2016). However, in Europe, it is particularly pervasive in hospital settings under national procurement regulations (Vogler and others, 2010). The practice of tendering has been analyzed extensively in many countries, focusing on its impact on the costs of different types of drugs, including biosimilars (Curto and others, 2014), vaccines (Garattini and others, 2012), retail pharmaceuticals (Danzon and others 2015; Kanavos and others, 2012), and especially hospital pharmaceuticals (Vogler and others, 2010; Vogler and others, 2013).

The procurement experiences in the Netherlands or Germany, where insurance companies use tendering systems to purchase drugs, are instructive and have been carefully studied. In the Netherlands, insurance companies determine the required medicines per population cluster for a given period in terms of active ingredient, dosage form and strength, and the medicines winning the tender are reimbursed (Kaplan and others, 2016). The insurer designates, for a period of six months, one or more preferred medication labels. The cheapest available product (branded or unbranded) is designated as the preferred product, together with all other products within a range of 5 percent in price. Products outside that range are not eligible for reimbursement (Kanavos and others, 2009). In Germany, the tendering system is used as a system to control cost and starts with manufacturers responding to an “invitation” to reduce their list price by providing a discount (or rebate) on that price (Kanavos and others, 2009). In both countries, the degree of centralization in the tendering system is organized at the level of the insurer, which operates at the national market level and thus can take advantage of economies of scale across a larger population group. However, the convenience and scope of the tender system needs to be adapted to the health system of each country.

Other interesting examples of the use of tendering in Europe are provided by Denmark, Belgium and Spain. In Denmark, the reimbursement system for outpatient pharmaceuticals follows a tendering scheme under which pharmaceutical companies submit every two weeks their price bids to the Medicines Agency, thus promoting a high degree of competition (Vogler and others, 2017). In contrast, in Belgium the tendering process was launched for only two medicines and in one of them the winner was a company with no capacity to procure and, as a result, the tender was abandoned (Kanavos and others, 2009). In Spain, with health competences at the regional level, the region of Andalusia designed a tendering system to contain pharmaceutical expenditures in outpatient medicines not through the choice of the product with lowest price (which is set at the national level) but through the choice of the medicine to be dispensed when prescribed or indicated by active ingredient (Espín and others 2019).

Studies generally find that tendering successfully lowers prices resulting in significant cost savings (e.g., Vogler and others, 2017; Carone and others, 2012; Kanavos and others, 2009). It also tends to increase the transparency of prices since the otherwise private discounts become directly observable through tendering (Carone and others, 2012). In some countries, as in The Netherlands, tendering very quickly resulted in fierce price competition amongst generic companies (Kanavos and others, 2009). While Wouters and others (2017) finds that the impact of tenders on prices may be durable, they also identify the need to carefully monitor the availability and prices of medicines to ensure continued access to affordable medicines for patients since there might be supply disruptions or shortages of medicines after tendering due, for example, to manufacturing disruptions among a small pool of suppliers (see also, Pauwels and others, 2014).

Unfortunately, there is little or no research on the long-term implications of such policies and their impact on doctors, the distribution chain and the generic and research-based pharmaceutical industry (Kanavos and

others, 2009). In the long run, it is important to pay attention to the number of manufacturers winning contracts. If that number decreases, monopoly power would increase and it would become necessary to watch for anticompetitive collusive behaviors that could increase prices (Danzon and others, 2015). Another issue worth exploring is the possibility of organizing a tendering system at the international level, in which insurers from a group of countries could set up a tender and possibly reap even greater benefits in terms of reduced prices (Carone and others, 2012). This type of international tendering system would be especially beneficial for smaller countries, and countries with limited technical capacity for more sophisticated cost containment measures, including LMICs.

B. Developing Economies

Improving access to medicines is crucial for achieving the universal health care objectives inherent in the Sustainable Development Goals (World Health Organization, 2018; Center for Global Development, 2019). In fact, even if health outcomes have lately improved in LMICs, change in health need, growing public expectations, and ambitious new health goals make necessary to place the focus on the development of high-quality health systems, producing better health outcomes and greater social value, with quality of care in the DNA of all health systems (Kruk and others, 2018). Thus, promoting quality use of essential medicines leads to better health outcomes and can achieve considerable efficiencies (Wirtz and others, 2017). Inefficient procurement and supply chain management have been identified as major challenges in many countries, where the special skills required for the procurement of quality assured products are lacking and stronger institutional infrastructure and accurate data management systems are needed in the supply chain (World Health Organization, 2018). This is key to ensuring equitable and affordable access to essential medicines for all, in a sustainable way, and assuring the quality and safety of medicines in order to prevent harm to patients (Wirtz and others, 2017).

Developing countries are facing a triple transition in their health systems (Center for Global Development, 2019). First, economic growth means that they need to prepare for a more limited role for donors in procurement. Second, they are experiencing an epidemiological transition from infectious to non-communicable diseases, which requires a different health care response and an evolving combination of drugs to be accessed by their population. Third, their health system organizations are moving away from disease-specific programs and out-of-pocket spending toward universal health coverage, with a greater commitment for governments to protect their citizens against catastrophic health spending. As a consequence, governments in LMICs must strengthen their capacity to procure medicines in a changing environment in which there are two decision levels, national and international, and where multilateral agencies play a significant role and some countries are decentralizing their procurement process to meet local needs (Center for Global Development, 2019).

The diagnostic on the existence of inefficiencies in procurement in LMICs is clear. First, the variance of prices for generic medicines is very high in LMICs. Second, deficient procurement systems lead to some of the

poorest countries paying some of the highest drug prices in the world for generics, with excessive purchase of more expensive branded generics as opposed to cheaper unbranded generics. Third, the heavy reliance on the private sector for medicine procurement means that public sector often does not have the capacity to effectively exercise monopsony power. Finally, the level of competition in the supply for essential medicines in LMICs is very low, with high market concentration (Center for Global Development, 2019). In an analysis of seven LMICs, Dubois and others (2019) find that, while there are clear benefits to pooling procurement, the reduction in prices when public procurement is centralized depends on the concentration of firms on the supply side and their market power. However, while tendering of pharmaceuticals results in cost reductions and greater price transparency (Kaplan and others, 2016), there is also evidence from Brazil (Bevilacqua, Farias and Blatt, 2011) that when not only price but quality standards are included in the tendering process, prices increased significantly because of the cost of the bioequivalence analysis to be performed and due to the insufficient presence of generics in the market. For that reason, it is recommended to impose quality standards in tendered procurement in order to attract multinational generic suppliers and reduce prices (Danzon and others, 2015). Center for Global Development (2019) also emphasizes the importance of strengthening the procurement systems in LMICs as well as supply-chain management, monitoring the market power in the supply of medicines in countries, and exploring possibilities for global cooperation in purchasing, e.g., international pooling.

Wouters and others (2019) provides an analysis of the experience of tendering in South Africa. In South Africa, tendering is operated by the government since 1982 for essential medicines and related products sold in all pharmacies in the public health care system. It consists of confidential bids by authorized manufacturers or importers for different categories of medicines, every two to three years. Importantly, quantities in the bid are not binding and afterwards the government may purchase a different amount. Price is the most important determinant of the bid winner, although there are other criteria.

Another important issue is the implications of trade agreements and the intellectual property (IP) rights for procurement policy. The TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement of the World Trade Organization (WTO) established minimum standards of protection that each government has to give to the IP of fellow WTO members, but it also incorporated some flexibilities to permit developing countries “to use TRIPS-compatible norms in a manner that enables them to pursue their own public policies, either in specific fields like access to pharmaceutical products or protection of their biodiversity, or more generally, in establishing macroeconomic, institutional conditions that support economic development” (World Intellectual Property Organization, n.d.). 't Hoen and others (2018) analyzed the implementation of such flexibilities in the agreements and found that TRIPS flexibilities have proven effective, especially for procuring generic versions of essential medicines. At the same time, it is recommended that these flexibilities be more consistently used for routine procurement (as opposed to as a last resort) in order to create and sustain generic competition.

VII. Policy Reforms and Data Availability

A range of policy measures can be used to promote more efficient use of pharmaceuticals. These include measures to reduce quantities by avoiding wasteful spending and lowering prices for new medicines.

A. Avoiding Wasteful Spending

The concept of efficiency in pharmaceutical expenditure can be understood as aiming to obtain the highest clinical outcome per monetary unit spent, by spending more only when it is necessary to obtain better health outcomes, and spending as little as possible for achieving a given level of health care. Efficiency requires both ensuring consumption efficiency and minimizing the cost of consumed medicines, which can be summarized in five rights: the right patient, the right drug, the right time, the right dose, and the right route (Grissinger, 2010), as both overuse of unnecessary medicines and underuse of necessary medicines may harm patients (Wirtz and others, 2017). In order to promote quality in the use of medicines, it is important to move from the goal of coverage to the measurement of effective coverage. For instance, in the case of HIV, the indicator could move from measuring the proportion of patients receiving antiretroviral therapy to the proportion of HIV patients with actual viral suppression (Kruk and others, 2018).

Efficient consumption requires efficiency in both the supply (by health professionals and pharmacies) and demand (by patients) of medicines through ensuring the appropriate prescription and use of medicines and adherence to treatments. There is evidence that improved communication between health professionals and patients (including through community programs) can reduce waste. On the demand side, cost sharing through copayments can promote efficient use. However, copayments require careful consideration in their design so as to avoid unintended consequences such as low or non-adherence to treatment by patients as prescribed or lead to inappropriate prescription, especially in low-income settings. Also, in order to make informed decisions about the purchase of medicines, it is important that both individuals and health systems get the right information about prices (Wirtz and others, 2017). An additional aspect to promote the efficient use of medicines is to increase the government capacity to regulate medicines to ensure safety and quality. On the supply side, financial incentives for health care providers in terms of some degree of responsibility for pharmaceutical expenditure may reduce wasteful prescription practices.

Policy #1. Invest to improve government capacities in terms of research and data analysis, regulation and evaluation of medicines, or designing and implementing pharmaceutical policy and procurement. This improvement in government capacity is especially important in LMICs so as to promote quality in the role of medicines in the health system.

Policy #2 Strengthen information systems, where feasible tracking pharmaceutical sales, prices, adequate prescribing and dispensing policies. The goal is to collect information to measure the quality in the use of medicines in health systems, moving from coverage to effective coverage measurements.

Analysis of that information would identify inappropriate use or misuse of pharmaceuticals and help in addressing this.

Efficiency also requires avoiding excess costs due to an inefficient mix of medicines or unnecessarily high prices. From this perspective, the promotion of generics is of primary importance and many countries are implementing such policies, albeit with varying success. Regulation should be focused on promoting early entry of generics once the patent is expired. Policies should encourage a sufficient degree of competition in the market in the long run so that the public sector benefits from significant cut in prices in the short run but also that these benefits are maintained in the long run. Transparency in prices also helps to promote competition. With respect to pricing, greater use of internal reference pricing (IRP) has proven to help reduce prices. Other successful policies include the mandatory prescription of INNs, incentives for doctors to prescribe generics, and making it mandatory to substitute with generics or providing incentives for pharmacies to dispense generics.

Policy #3. Improve data regarding the implementation of policies promoting generics and their characteristics (interchangeability, incentives in prescription, mandatory substitution, etc.) to help identify whether policies are the most appropriate given the socioeconomic and geographic situation of each country. In general, generic substitution, a reference price (IRP) for a group of interchangeable medicines, and prescription using International Non-proprietary Names (INN) are recommended policies.

Policy #4. Provide educational programs to the different stakeholders (physicians, pharmacists, health policy makers, but also to a broader population) to overcome reluctance to generics.

Procurement should be designed to guarantee availability of all needed drugs in the long run and at the lowest feasible price, allowing for incentives for research and development. In developed countries, tendering is a very common practice, especially for off-patent medicines. Although it is very effective in reducing prices, it is important to preserve a high degree of competition among suppliers over the long run to help guarantee availability of products and avoid supply disruptions or shortages. Because of economies of scale, pooled and collaborative procurement at the national (or even supranational) level should produce savings. In developing countries, it is necessary to build the capabilities in the health system to design a more efficient procurement system, with a higher presence of non-branded generics and a greater degree of competition among suppliers.

Policy #5. Improve data on the tendering systems used, and their key variables (type of pharmaceutical products and providers, price, concentration index, quality assurance, capacity and possibility of supply disruption, national/regional scope) to help identify any deviation from the benchmark. In general, a centralized tendering system is recommended. In the case of small countries or with limited technical capacity for more sophisticated cost containment measures or LMICs, an international tendering system is recommended.

Policy #6. Assure the coverage of essential medicines in the benefit package by the health system, regulate their price and reduce the amount of out-of-pocket spending on medicines, so as to make them affordable, especially for those in need and in LMICs.

B. Innovative Medicines and Their Pricing

Health systems should promote the early introduction of innovative pharmaceutical products to maximize the clinical benefit of those products at a price that takes into account short and long run effects. Prices should be low enough to guarantee sustainability of health systems, but also high enough to promote R&D innovation (Scannell and others, 2012; Belloni and others, 2016). Furthermore, it is important to orientate innovative efforts towards the medicines that the international community considers are most needed.

In the case of innovative and expensive drugs protected by patents, many countries use external reference prices and cost-effectiveness analysis for setting their price and reimbursement. It is important to adapt the pricing policy to the socioeconomic status of the country. External reference price (ERP) systems help to contain costs through lowering prices. However, the common use of confidential discounts may distort the benefits of ERP. For example, when used in high-income countries it may reduce prices in the short run but at the cost of lowering incentives for research and development in the long run, and it may lead to strategic behavior by manufacturers in the form of launch delays that may affect lower-income countries. When used, to help in the decision making at the payer level but also reducing uncertainty for the manufacturers, ERP systems should be transparent, simple, stable, and sustainable. The use of ERP is more justified in countries facing difficulties in implementing cost-effectiveness analysis in price setting.

Policy #7. Create an Essential Medicines Patent Pool at the international level to orientate the efforts of research and development.

Policy #8. Improve data on the utilization of ERP per country and its characteristics (number of countries taken into account and which ones, algorithm used, etc.), crossed with information about the price of medicines reimbursed (as in the mentioned EURIPID database) to help identify inefficiencies in the system. In general, a transparent, simple, stable and sustainable ERP system is recommended for developing countries.

Health technology assessment and cost-effectiveness analysis are tools for setting prices for innovative drugs that better reflect their value (Value Based Pricing) and are thought to be the superior approach for the promotion of value for money (Drummond and others, 2011; Atun, 2015). The UK is a useful example of a country that routinely uses cost-effectiveness analysis. It is recommended for countries with the capability of developing the needed sophisticated data and analysis, taking account of possible strategic behavior of manufacturers. Also, international cooperation in terms of information sharing and data generation is recommended to improve the bargaining power of governments.

Policy #9. Improve data on the utilization of VBP, MEA or SDF with their characteristics (for instance, VBP using mandatory cost-effectiveness analysis, or a threshold of the incremental cost-effectiveness ratio; MEA being confidential or public, using price–volume agreements, or performance-based schemes; SDF defined by a specific budget) to help compare the different uses and identify deviations from the benchmark. In general, VBP is recommended if feasible, especially for developed countries. With respect to SDF, if used, it is suggested to use the ‘only in research’ recommendation restricting financed use of the drug to research that can resolve uncertainties.

Policy #10. If VBP is implemented, it is recommended to link the appraisal of the costs and benefits of new drugs with national rebate agreements.

C. Pharmaceutical Expenditures in Hospitals and Biosimilars

Most of the information available regarding pharmaceutical expenditure at the international level refers to retail pharmaceutical products. However, over recent years, pharmaceutical expenditure in hospitals is growing faster than in retail. Yet, not all countries report pharmaceutical expenditures following the same criteria, which makes analysis difficult. Procurement by hospitals is increasingly important and the design of such procurement might benefit from economies of scale through increased market (monopsony) power in demand and through greater transparency in prices.

Policy #11. Improve the availability of data on pharmaceutical expenditures in hospitals to help enhance our understanding of how these pharmaceutical expenditures differ across countries.

Many of the new innovative and expensive products behind increasing expenditure are biological medicines. When the patent of a biological originator expires, the market is open for the entry of biosimilars. A biosimilar is a biological medicine that demonstrates sufficient similarity to the biological originator in quality characteristics, biological activity, safety and efficacy. In Europe, the first biosimilar was authorized in 2006 (somatropin), and since then 67 biosimilar medicines have been authorized centrally by the European Medicines Agency⁷ (EMA) (European Medicines Agency, 2022), i.e., authorized and neither withdrawn nor refused, corresponding to 17 active ingredients. In 2018, in Europe, over 30 percent of all drug spending was on biological medicines, of which 1.5 percent are biosimilars (IQVIA Institute, 2019), and this market is significantly increasing. In the US, in contrast, licensing biosimilars is possible since 2010, but the first biosimilar was only approved in 2015 (Belloni and others, 2016). All biological medicines inherently carry a certain degree of variability, and there may be small differences between different batches of the same biological medicine (European Commission, 2017). Although it is not an exact copy (as for the case of the generic) with respect to the chemical originator, their biosimilarity provides expectations about their entry in the market resulting in significantly lower prices for

⁷ Updated information available [here](#).

biological pharmaceuticals and increasing access. However, because development costs of biosimilars are much higher than those of generics, the expected impact on prices is lower. Data from five European countries (France, Germany, Italy, Spain, and the United Kingdom) and the United States suggests that there has been a 20 percent reduction in price per treatment-day across eight products which could result in cumulative savings exceeding EUR 50 billion by the end of 2020 (OECD, 2017). Also, in Spain, García-Goñi and others (2021) estimate that in 2019, the savings derived from the use of biosimilars relative to total pharmaceutical spending was of 3.92%. To date, lack of data makes it infeasible to perform an analysis of the economic impact of biosimilars on pharmaceutical spending in hospitals similar to the one performed above for generics in pharmaceutical spending in retail.

Policies implemented to promote generics could also be used for the promotion of biosimilars. In particular, it is important to know the position of regulators regarding the interchangeability between biologics and biosimilars and, in Europe, the EMA allows countries to individually decide on that matter (Ekman and others, 2016). Policies implemented in each country are different, as has been the evolution of the uptake of biosimilars. In Norway and Denmark, biosimilars were strongly promoted by health authorities since their beginning, and tenders were set at the national level, while in countries such as Italy health authorities have been more conservative, and the uptake has been slower (IQVIA Institute, 2018). In 2017, the market share of biosimilars in the molecule of Anti-TNF alfas was 93 percent in Norway and 94 percent in Denmark, while it was only 35 percent in Italy and 26 percent in France (OECD, 2019). Norway is a good example in the uptake of biosimilars, with a combination of policies related to pricing and national tendering, uptake enhancement, and education (Vogler and others, 2017). Also, as Ferrario and others (2020) point out, early market entry and rapid uptake of quality assured generics and biosimilars are key to improving access to medicines. Although more research is needed, biosimilars represent a great opportunity for enhancing the sustainability of health systems through rationalizing pharmaceutical spending (García-Goñi and others, 2021).

Policy #12. Improve the availability of international data on market share of biosimilars (volume and sales) to help analyze this market, evaluate policies (interchangeability, tendering, information), and estimate the savings from the uptake of biosimilars.

Policy #13. Provide educational programs to the different stakeholders (physicians, pharmacists, health policy makers, but also to a broader population) to overcome reluctance to biosimilars to promote their use. Regulate the participation of biosimilars in the tendering system.

VIII. Conclusion

Pharmaceutical spending has increased considerably worldwide in the last few decades. While the positive impact of increased access to pharmaceutical products for the functioning of health systems and in increasing life expectancy or quality of life is unquestionable, it comes at a substantial direct cost. Hence, pharmaceutical expenditure has become a concern, and many countries have implemented various policies focused on containing costs and promoting more efficient use of medicines.

This paper discusses the economics of pharmaceuticals, the incentives associated with their demand and supply, the databases that may be relevant in the design of pharmaceutical policies, and the trend in the main indicators of pharmaceutical expenditure. **Our empirical analysis suggests that increasing the volume market share of generics in retail is associated with significant efficiency gains in terms of pharmaceutical spending, and releases resources to be allocated either within the health sector or to other sectors, thus increasing the value for money.** We also provide a simulation of those savings for a set of countries. The paper then reviews the main policies being implemented to reduce waste in medicines, control prices, promote generics and early access of innovative products, avoid abusive consumption, and improve procurement practices.

Incentives for innovation in the long run, early access of innovative products with value-based prices, and promotion of generics and biosimilars are key objectives. Inefficient procurement and tendering may lead to high prices or shortages with the consequent reduction in access. Its design needs to account for the quality of products, the degree of competition and concentration index in supply, market power on the demand side, and the level of fragmentation in the health system. This is especially important in developing countries, where access is necessary for survival, while in the case of developed economies those inefficiencies lead to excessive pharmaceutical expenditure. An inappropriate use of external reference price systems may lead to strategic delays in the launch of innovative products in poorer countries and, where feasible, prices of innovative products should be set using cost-effectiveness analysis so that manufacturers obtain the right incentives for productive research and development. Financial incentives and the organization of health systems with respect to health services provision and pharmaceuticals use are important to promote incentives for efficiency and avoid waste, and any cost-sharing policy needs to be directed to reduce abusive consumption while guaranteeing the appropriate adherence to prescribed consumption advice.

A key constraint for policy analysis and advice is the lack of data at the international level regarding the growing market **of pharmaceuticals in hospitals** and, in particular, **for biological products (originators and biosimilars).** Although there are well-known differences between the markets for generics and biosimilars, it is expected that biosimilars play an important role, comparable to that of generics, in lowering prices and expanding access to biological pharmaceuticals. **Although still small, this market and the policies being pursued, should receive increased attention. Future research is needed to perform an analysis of pharmaceutical expenditures in hospitals and of purchasing and pricing practices.**

We propose various pharmaceutical policies intended to rationalize pharmaceutical spending, guarantee the equitable and affordable access for all to essential medicines, and ensure the access of innovative medicines to the market in a sustainable way. However, it is important to note that many of these policies may require substantial change of regulatory environment of countries, and the understanding and support of both the government and appropriate government agencies (such as the Ministry of Finance, Ministry of Economy, Treasury, National Procurement body, or the National Health Insurance Agency). To that end, it is crucial to improve government capacities where needed.

In summary, governments must be continually active in reviewing the policies they and other actors are pursuing with respect to pharmaceutical spending. The goal should not be understood as simply cutting spending, but as promoting the greatest possible access with efficient and rational use of resources, without reducing health outcomes, to produce efficiency gains for the entire economy.

Annex I. Analysis of the Impact of the Market Share of Generics in Pharmaceutical Spending

Annex Table A1.1. Regression Analysis on the Impact of the Volume Share of Generics on Pharmaceutical and Health Expenditures

	Pharmaceutical Expenditures			Share of Pharmaceutical Expenditures with respect to Health Expenditures			Health Expenditures per capita (PPP)			Share of Health Expenditures with respect to GDP			Share of Pharmaceutical Expenditures with respect to GDP		
	Coef.	Std.Err	P> t	Coef.	Std.Err	P> t	Coef.	Std.Err	P> t	Coef.	Std.Err	P> t	Coef.	Std.Err	P> t
Increase of 10% in Share of GDP per capita	-35.88	0.50	0.00	0.52	0.02	0.00	-48.48	3.11	0.12	-0.23	0.00	0.00	-0.05	0.00	0.00
Austria	54.25	22.13	0.02	-0.70	0.67	0.30	1045.64	145.06	0.00	0.11	0.23	0.63	-0.07	0.06	0.20
Belgium	42.64	26.80	0.11	3.13	0.81	0.00	602.80	172.63	0.00	-0.89	0.27	0.00	0.04	0.07	0.57
Denmark	-195.35	20.18	0.00	-5.35	0.61	0.00	457.55	132.28	0.00	1.45	0.21	0.00	-0.37	0.05	0.00
France	76.85	29.25	0.01	3.03	0.89	0.00	867.47	189.65	0.00	-0.09	0.30	0.76	0.18	0.08	0.02
Germany	253.66	27.00	0.00	-0.58	0.82	0.48	1430.12	174.26	0.00	1.00	0.28	0.00	0.28	0.07	0.00
Greece	6.92	54.97	0.90	17.00	1.66	0.00	-904.54	350.60	0.01	-5.58	0.56	0.00	0.50	0.14	0.00
Ireland	-14.90	23.38	0.53	2.74	0.71	0.00	262.67	149.49	0.08	-0.33	0.24	0.17	0.03	0.06	0.62
Italy	-26.57	37.80	0.48	6.97	1.14	0.00	-86.16	243.55	0.72	-3.26	0.39	0.00	-0.03	0.10	0.76
Luxembourg	-230.92	66.37	0.00	0.30	2.01	0.88	-607.54	414.84	0.14	1.53	0.66	0.02	-0.05	0.17	0.78
Netherlands	-12.93	20.30	0.53	-4.93	0.61	0.00	1096.18	133.40	0.00	0.69	0.21	0.00	-0.28	0.05	0.00
New Zealand	-	-	-	-	-	-	308.56	227.48	0.18	-1.61	0.36	0.00	-	-	-
Portugal	-23.48	48.08	0.63	6.15	1.46	0.00	-18.62	308.72	0.95	-3.62	0.49	0.00	0.03	0.12	0.80
Slovak Republic	176.72	55.44	0.00	15.23	1.68	0.00	-238.10	352.63	0.50	-5.78	0.56	0.00	0.42	0.14	0.00
Spain	-4.14	38.71	0.92	6.47	1.17	0.00	-72.78	249.51	0.77	-3.60	0.40	0.00	-0.04	0.10	0.70
Switzerland	204.21	34.04	0.00	3.22	1.03	0.00	1246.75	186.73	0.00	3.78	0.30	0.00	0.57	0.09	0.00
Turkey	-	-	-	-	-	-	-1370.54	389.31	0.00	-9.43	0.62	0.00	-	-	-
United Kingdom	44.03	34.33	0.20	-1.72	1.04	0.10	154.41	196.65	0.43	-1.64	0.31	0.00	-0.05	0.09	0.60
2001	30.53	21.60	0.16	0.21	0.65	0.75	131.66	126.53	0.30	0.25	0.20	0.21	0.05	0.06	0.38
2002	74.00	21.64	0.00	0.53	0.66	0.42	339.45	123.80	0.01	0.52	0.20	0.01	0.12	0.06	0.03
2003	92.76	20.58	0.00	0.30	0.62	0.63	412.60	121.92	0.00	0.93	0.19	0.00	0.18	0.05	0.00
2004	122.52	20.53	0.00	-0.70	0.62	0.26	582.04	122.11	0.00	1.31	0.19	0.00	0.21	0.05	0.00
2005	143.61	20.99	0.00	-1.06	0.64	0.10	633.71	125.21	0.00	1.48	0.20	0.00	0.23	0.05	0.00
2006	164.82	21.60	0.00	-1.66	0.65	0.01	748.04	129.26	0.00	1.61	0.21	0.00	0.22	0.06	0.00
2007	193.64	21.92	0.00	-1.96	0.66	0.00	868.15	132.14	0.00	1.77	0.21	0.00	0.24	0.06	0.00
2008	225.11	22.12	0.00	-2.63	0.67	0.00	1167.24	130.48	0.00	2.20	0.21	0.00	0.25	0.06	0.00
2009	236.85	21.70	0.00	-3.30	0.66	0.00	1379.22	127.31	0.00	2.76	0.20	0.00	0.30	0.06	0.00
2010	249.05	22.29	0.00	-3.69	0.68	0.00	1463.30	131.92	0.00	2.79	0.21	0.00	0.27	0.06	0.00
2011	241.80	22.90	0.00	-4.17	0.69	0.00	1463.07	135.89	0.00	2.75	0.22	0.00	0.23	0.06	0.00
2012	253.01	23.36	0.00	-4.97	0.71	0.00	1637.38	138.87	0.00	2.92	0.22	0.00	0.21	0.06	0.00
2013	272.82	23.97	0.00	-5.17	0.73	0.00	1754.55	143.25	0.00	2.97	0.23	0.00	0.19	0.06	0.00
2014	276.61	24.98	0.00	-5.43	0.76	0.00	1783.66	149.37	0.00	2.99	0.24	0.00	0.17	0.06	0.01
2015	296.95	25.99	0.00	-5.35	0.79	0.00	1823.43	155.89	0.00	3.02	0.25	0.00	0.19	0.07	0.01
2016	316.84	26.56	0.00	-5.34	0.80	0.00	1938.75	159.90	0.00	3.15	0.25	0.00	0.21	0.07	0.00
2017	328.61	27.07	0.00	-5.54	0.82	0.00	2038.50	163.46	0.00	3.19	0.26	0.00	0.20	0.07	0.01
2018	337.76	48.18	0.00	-5.37	1.46	0.00	2087.49	186.19	0.00	3.06	0.30	0.00	0.21	0.13	0.10
constant	321.09	73.17	0.00	14.59	2.22	0.00	537.52	465.30	0.25	13.90	0.74	0.00	2.01	0.19	0.00
N	206			206			255			255			206		
Adj. R-squared	0.8977			0.9612			0.9575			0.938			0.9369		

*Australia: omitted by construction

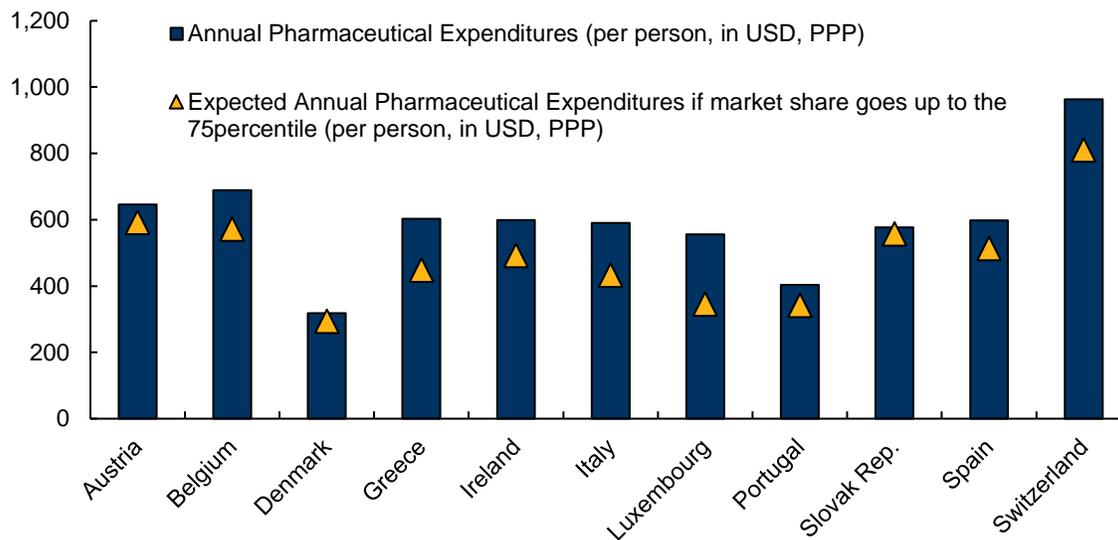
Annex Table A1.2. Current and Simulated Market Volume Share of Generics

(Simulation Increases Market Share to the 75 Percentile (70.05 Percent))

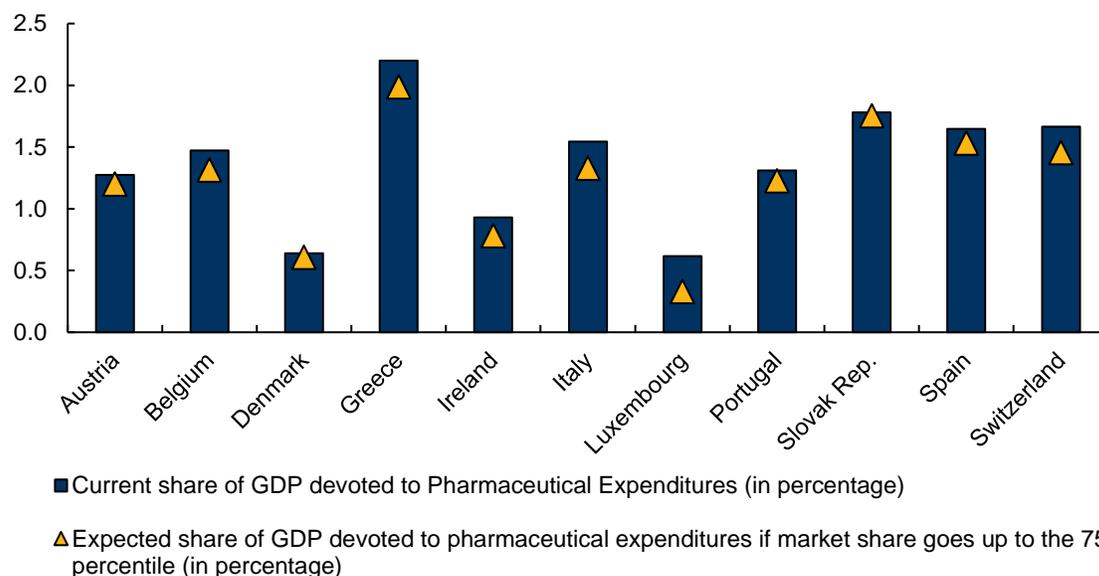
Country	Real market share of generics (volume)	Market share if when lower increased to the 75th percentile
Austria	54.8	70.05
Belgium	37.3	70.05
Denmark	63.2	70.05
Germany	82.3	82.30
Greece	26.8	70.05
Ireland	40	70.05
Italy	26.2	70.05
Luxembourg	11.3	70.05
Netherlands	75.6	75.60
New Zealand	80.5	80.50
Portugal	52.8	70.05
Slovak Rep.	64.5	70.05
Spain	46.4	70.05
Switzerland	27.3	70.05
Turkey	59	70.05
United Kingdom	85.3	85.30

Annex Figure A1.1 Savings in Retail Pharmaceutical Expenditures

(when Market Share of Generics is Increased to the 75 Percentile: in USD PPP, 2017)

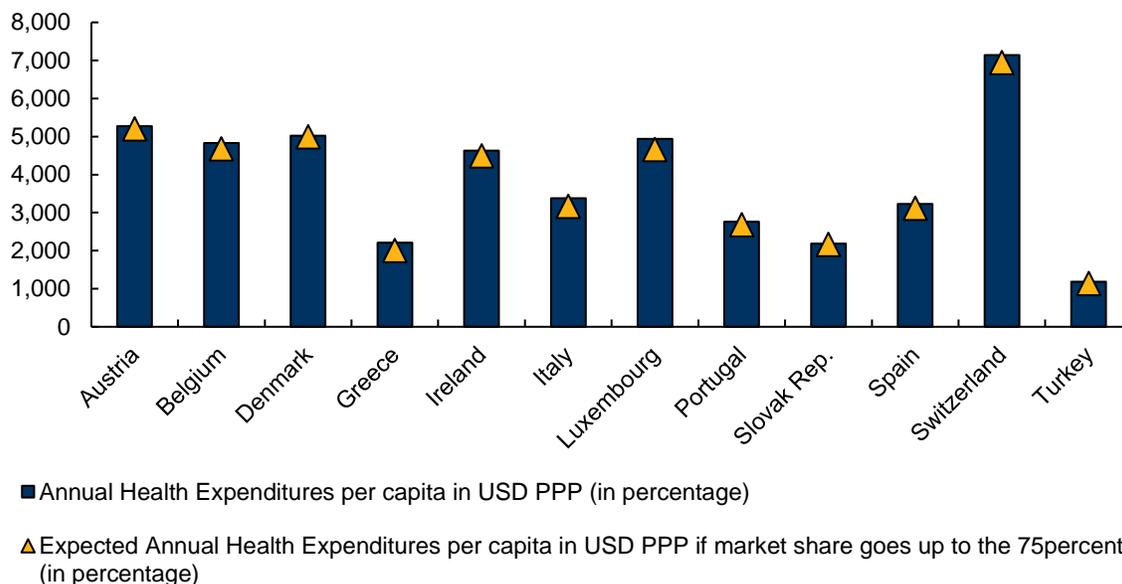


Annex Figure A1.2. Efficiency Gains by Reducing the Share of GDP Devoted to Retail Pharmaceuticals
(when Market Share of Generics is Increased to the 75 Percentile: in Percentage, 2017)

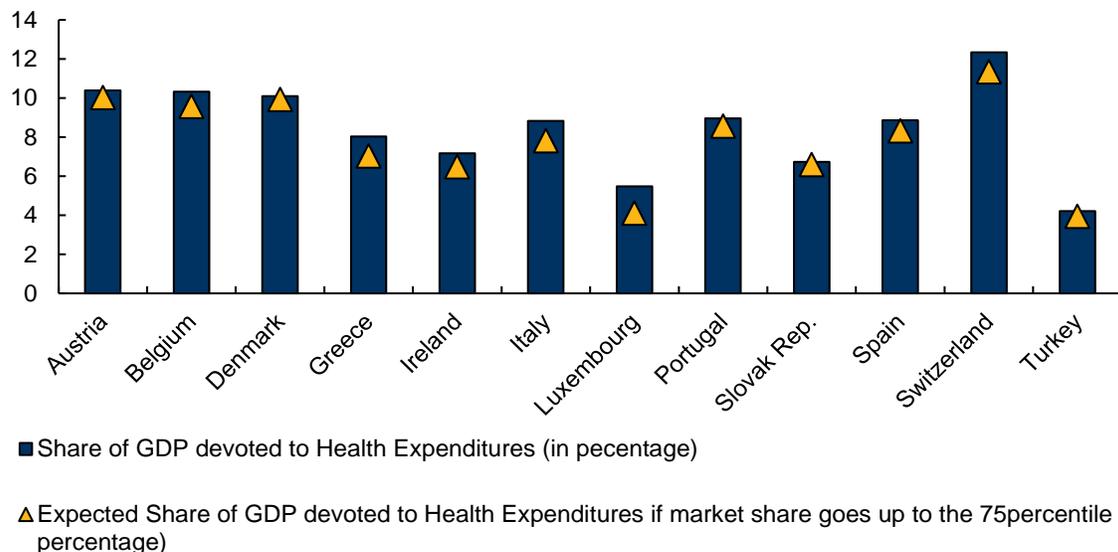


Annex Figure A1.3. Savings by Reducing Health Expenditures per Person

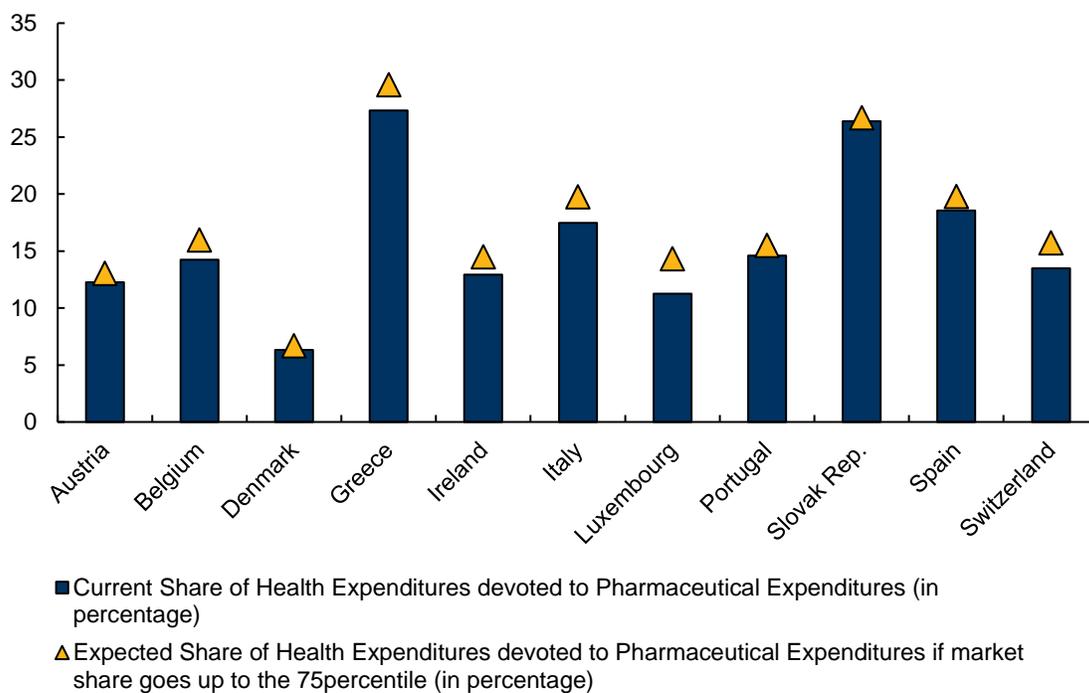
(when Market Share of Generics is Increased to the 75 Percentile: in USD, PPP, 2017)



Annex Figure A1.4. Efficiency Gains by Reducing the Share of GDP Devoted to Health Spending
(when Market Share of Generics is Increased to the 75 Percentile: in Percentage, 2017)



Annex Figure A1.5. Change in the Share of Retail Pharmaceutical Expenditures in Health Expenditures
(when Market Share of Generics is Increased to the 75 Percentile: in Percentage, 2017)



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