Haute Ecole
Groupe ICHEC – ECAM – ISFSC

Enseignement supérieur de type long de niveau universitaire

Vaccines Pricing Transparency in Europe

A path for fair price and more accessibility

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Pour l'obtention du diplôme de
Master en gestion de l'entreprise - tridiplomation

Année académique 2020-2021

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Abstract

The present thesis focuses on the investigation of whether more transparency in vaccine pricing can lead to more fair and lower prices, promoting more vaccination access to European citizens. As health is a fundamental right and vaccines are one of the most cost-efficient health tools to ensure this right, the discussion on perception of fairness and price balance from different theories of justice put it in perspective. The vaccine industry is inserted in a landscape of high heterogenic regulation, uncertainty on return of investment, and operates in a concentrated market in both supply across few multinational biopharmaceutical companies and in demand mainly from public buyers. As a result, the research, development and production of a vaccine have been lengthy, bureaucratic and expensive, reasons as to why the discussion regarding transparency is pertinent in this complex dynamic.

KEYWORDS: vaccine; pricing; transparency; fairness; healthy policy; Europe.

Acknowledgements

I would like to thank my thesis promoter, Dr. Géraldine Thiry, for her invaluable supervision, helping to structure academically my storm of thoughts during the course of this master's degree. My gratitude extends to Nayoung Sarah for her unconditional support proof-reading and checking language errors in challenging deadlines.

Special thanks to Bhevan Chandrasena for opening the doors for me to the pharmaceutical world and to Mayra Souza for her constant mentoring which influenced my academic and career development positively. Additionally, I would like to express gratitude to Juliana Dal Pino for our treasured talks about the health market that helped me to have different perspectives of the health industry.

My appreciation also goes out to my family and friends in Brazil and Belgium, especially to Marta, Carolina, Antoine, Lísia and Reham for their encouragement and support all through my studies.

Conflict of interest statement

The views and opinions expressed in this manuscript belong to the author alone, and do not represent the views, policies, and opinions of any current or past employer. The author wrote this thesis while employed by GlaxoSmithKline, a relevant vaccine manufacturer, in the past as an intern at Baxter, a leader in sterile medication production.

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Acronyms

AFR/AFRO - WHO African Region
AMC – Advance market commitments
AMF – Access to Medicine Foundation
AMR/AMRO - WHO Region of the Americas
aP-containing - acellular pertussis–containing
APC – Advanced purchase commitment
BBIL - Bharat Biotech International Ltd
BCG - Bacillus Calmette–Guérin (for tuberculosis)
bOPV - Polio vaccine – oral (OPV) bivalent types 1 and 3
CBA – Cost -benefit analysis
CEA – Cost-effectiveness analysis
CEPI - Coalition for Epidemic Preparedness Innovations
CESCR – Covenant on Economic, Social and Cultural Rights
CHMP – Committee for Medicinal Products for Human Use
CUA – cost-utility analysis
DALY – disability- adjusted life years
D&T- Diphtheria- and tetanus-containing
DCVM(s) - Developing country vaccine manufacturer(s)
DGHFS - Directorate-General for Health and Food Safety
DtaP - Diphtheria-tetanus-pertussis (acellular)
DTwP - Diphtheria-tetanus-pertussis (whole cell)
EAHC - Executive Agency for Health and Consumers
EC – European Commission
ECDC - European Centre for Disease Prevention and Control
EEA- European Economic Area
EHFG - European Health Forum Gastein
EMA - European Medicines Agency
EMR/EMRO - WHO Eastern Mediterranean Region
EP – European Parliament
EPHA- European Public Health Alliance
EU – European Union
EUR/EURO - WHO European Region
FDA - U.S. Food and Drug Administration
GAVI - Global Alliance for Vaccines and Immunization
GDP – Gross Domestic Product
GNI - Gross national income
GSK – GlaxoSmithKline
GVAP - Global Vaccine Action Plan
GVMM - Global Vaccine Market Model
H1N1 - hemagglutinin type 1 and neuraminidase type 1(swine flu)

HepA, HepB - Hepatitis A, hepatitis B
Hib - Haemophilus influenzae type b
HIC(s) - High-income country/ies
HPV - Human papillomavirus
HTA- Health Technology Assessments
IHSI - International Horizon Scanning Initiative
IPV - Inactivated Polio Vaccine
IVIR-AC - Immunization and Vaccine-related Implementation Research (IVIR) Advisory Committee
JE - Japanese encephalitis
JPA – Joint Procurement Agreement
JRF - Joint Reporting Form
MCV(s) - Measles-containing vaccine(s)
MCV2 - Measles-containing-vaccine second-dose
MenA, Men B, MenC - Meningococcal A, B, C
MenACW-135 (Ps) - Meningococcal ACW-135 polysaccharide
MenACWY - Meningococcal ACWY
MI4A – Market Information for Access to Vaccines
MIC(s) - Middle-income country/ies
MLR – Multiple linear regression
MMR – Measles, Mumps and Rubella
MMRV - Measles, mumps, rubella and varicella
MR - Measles and rubella
mRNA- messenger ribonucleic acid
MSF – Medicine Sans Frontiers
NIP(s) - National immunization program(s)
NITAG - National immunization technical advisory group
NRA(s) - National regulatory authority/ies
OCV - Oral cholera vaccine
OPV - Oral polio vaccine
PACE – Parliamentary Assembly Council of Europe
PAHO RF - Pan American Health Organization Revolving Fund
PCV - Pneumococcal conjugate vaccine
PDP – Product Development partnership
PoS – Probability of success
PPSV - Pneumococcal polysaccharide vaccine
PQ'd - Prequalified
Ps - Polysaccharide
R&D- Research and Development
Rota- Rotavirus
QALY – quality adjusted life years
SAGE – Strategic Advisory Group
SCP – Structure, Conduct and Performance

SE - South-East
SEAR/SEARO - WHO South-East Asia Region
SII - Serum Institute of India
SIA - Supplementary immunization activities
SMA – Spinal Muscular Atrophy
TBE - Tick-borne encephalitis
TCV - Typhoid conjugate vaccine
Td - Tetanus-diphtheria (reduced antigen content)
Tdap - Tetanus-diphtheria-acellular pertussis (reduced antigen content)
TT - Tetanus toxoid
TTP – Target product profile
UDHR – Universal Declaration of Human Rights
UMIC - upper-middle-income country
UN- United Nations
UNICEF - United Nations Children's Fund
UNICEF SD - United Nations Children's Fund Supply Division
V3P - Vaccine Product, Price and Procurement
WHO – World Health Organization
WHO SE- South-East Asia Region
wP - whole-cell pertussis
WPR/WPRO - WHO Western Pacific Region
YF - Yellow fever

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1. Introduction

1.1. Context

Europe has the highest life expectancy in the world, as the demands of the health market increase and evolve, and the European health care systems become more fragile due to pressures to balance public revenue and expenses. Vaccines are well recognized as one of the most cost-efficient health solutions, preventing about 2.5 million deaths worldwide per year (EU, 2019, p.18), and accordingly reducing the burden on health costs.

But the higher prices have been charged for vaccines along the past decades (IM, 2003 p. 128) started to raise concerns on its fairness and affordability, especially flagging disproportional soaring profits for manufacturers. Through the recent pandemic of Covid-19 in 2020, governments and society realized the importance of vaccination not only because it is preventing communicable diseases but also because health is a driver of economic development. The cost of inaction in health can be dreadful, in terms of both human lives and economic impact. Boosting immunization coverage or reshaping vaccine markets to guarantee safe and effective vaccines that are readily available and affordable should be promoted by all stakeholders as a way to ensure the right to health in Europe.

How much is fair to pay for a vaccine that can save your life? In a pandemic, it is fair to set up prices based on the willingness to pay of citizens or countries? These questions gained additional importance as the world is currently living a Coronavirus pandemic of with 3.3 million deaths, of which 1.1 million are from Europe as of 12th May 2021 (ECDC, 2021). Understanding how fairness is perceived through ethical theories of justice would help to put into perspective the different arguments. A fair price to pay for a vaccine would be the amount setup in a level to ensure the achievement of this fundamental right for the most vulnerable, and not only to the countries or citizens able to afford high priced vaccines.

The greatest challenge is how to balance pricing with fairness, innovation, as well as political and economic interests from multiple stakeholders.

The vaccine business has a complex and unique landscape, from research and development to manufacture and adoption in a country's immunization agenda. The cycle is long (about 8 -15 years for a non mRNA vaccine), bureaucratic (highly regulated by heterogenic rules), risky (uncertainty of successful vaccine candidate and future demand), and expensive (R&D and manufacturing costs require sustained mobilization of highly skilled human and financial resources over a long period of time).

From an economic perspective, all these barriers and risks should be compensated by a higher return and thus higher prices, to attract and keep private companies motivated to stay in the market producing vaccines. However, this risk-incentive model is underpinning great criticism

on the biopharmaceutical companies due to the eventual and unethical increasing of prices, which is kicking off conversations about new ways to incentivize R&D on health solutions.

Not only the manufacturers have importance in the market dynamics, but also the governments and public institutions (e.g., the EU) have an essential role on the vaccine cycle, whether by regulating safety or being the main source of vaccine demand through inclusion into national vaccination agendas.

Accordingly, the limited number of vaccine buyers and sellers leads to a tenuous balance between demand and supply in vaccine markets and so aggregates elements to jeopardize the fair pricing of immunizing products.

1.2 Hypothesis

To manage and finance health solutions, the countries have been exploring different strategies to reduce health expenditure such as health technology assessment, regulatory flexibilization and exchange, collaboration on price scanning, price negotiations, pooled procurement, etc.

In the current work the hypothesis investigates whether transparency in vaccine price in European Union countries can:

i) increase the perception of price fairness;
ii) lower prices, enabling more accessibility of vaccines to society.

1.3 Research Questions

The present research is an investigation into vaccine pricing practices underpinned by two main assumptions regarding to perception of fairness and lower price, and accessibility.

In order to pave the way to an answer to these assumptions, this thesis elaborated ways to understand why vaccine prices are high, and what factors could explain that pricing transparency is low; these two questions are very meaningful if one first understands why prices matter.

These three questions were chosen to better build a narrative, passing by critical points often considered by authors as grey zones.

Fair prices are important because it suggests affordability of a fundamental human right, which is health. Guaranteeing access to life transforming health commodities like vaccines is a challenge for EU health policies.

From the last decades the prices of vaccines are considered high, so understanding what is the background and the dynamics which are contributing to the current price levels would help to think of solutions to improve it by lowering prices.

Finally, one of the most polemic topics among literature is the public disclosure of prices paid by the governments for the vaccines. The respective research question aims to underline what are the elements contributing for such low levels of transparency and assess if more disclosure would affect vaccine pricing.

1.4 Methodology

In order to satisfy the objectives of this dissertation, a qualitative research was held to better describe and analyze the research questions.

It is important to mention that the effectiveness of a qualitative research is mainly based on the skills and abilities of researchers on the same field of the present investigation, then outcomes may not be perceived as conclusive or impartial because of eventual personal interpretations. Thus, to balance and be the most impartial as possible we offer different positions and counter-arguments for the main research questions, giving a broader overview of the transparency in pricing.

Equally, the nature of the topic involves confidential data (such as vaccine prices), causing limitation on the material available, whether qualitative or quantitative.

The data collection for this research was done primary from WHO, EU agencies, European Parliament and foundations such as reports, policy papers, governmental publications because of the nature of the research topic – regulated and often confidential. Secondary sources were from relevant literature and informal interviews with workers of pharmaceutical companies (which were not published in this thesis to avoid conflict of interest. Those interviews were used only to support the author to have broader lines of argumentation to be searched in public databases).

The subsequent data analysis used a qualitative analysis through a non-systematic literature review and a market assessment of the vaccine industry was performed through analytical support of the Structure-Conduct-Performance (SCP) paradigm.

The collection and evaluation of the data faced challenges: theoretical arguments and correlations explored were often inconclusive, and there are not many real case examples on whether greater price transparency would lead to higher or lower vaccines' prices or trigger more fairness to European citizens available in literature. The recognition of such scarcity of scientific materials shows how indeed the public disclosure of prices are low, strengthening the relevance of the research questions.

1.5 Structure

Chapter 2 contains the normative justification of this thesis subject. It aims to clarify what the main discussions in regards to fair price are and why it is important to spotlight it. It points out health as a fundamental human right with the legal evolution. An important emphasis was given on how fair price is perceived on health products by consumers, passing through the discussion on whether health is seen as a commodity for trade and its sensitivity in peaks of demand without proportional supply. Further, it explores ways to have equal distribution of the benefits from trade and vaccine accessibility through ethics perspective with support of theories such as Utilitarianism, Libertarianism and Rawls' justice theory.

Chapter 3, it finds a framework of the European health system specifically touching the vaccines, in which outlines the important role of the public government (EU or Member-States) because of its influence in the vaccine market as a regulator and main consumer. This session analyses the level of vaccine demand concentration and levels of regulation in the industry.

Chapter 4 elaborates ways to understand the reason of high vaccine prices, with a broader view of its complexity: since the conceptual idea and its research and development, and its manufacture, distribution, and finally the administration on the final user. Elements of the vaccine price such as the firm's strategy, evaluation by governments and price correlations were described to enrich the research with the perspective of different stakeholders. The market dynamics were captured through the support of SCP paradigm as an analytical framework to inform the main variants in the industry that are collaborating to keep the vaccine's price in such patamar.

Chapter 5 contains the factors that helps to understand the current low level of pricing disclosure to society. This session assesses by literature review whether more transparency in the prices paid by public buyers and in other key pricing elements would influence the market dynamics to mitigate the effects on the asymmetric information by a certain extent to lower the prices of vaccines in the EU.

2. Fair price

Life. How much are you willing to pay for something that can save your life? Another pertinent question is how much is fair to pay for something that can save millions of lives?

There are several ways to approach the answers: by economic theories of supply and demand, elasticity of prices, market power, philosophical notions, theories of justice, etc. The way chosen in the current argumentation of whether more transparency in vaccine prices would promote more fair prices is mainly through ethics. And for this purpose will be established a connection on the elements of price that could lead to more transparency on its setup and therefore a lift on fairness between stakeholders and accessibility to ensure more citizens the human right of health.

An ethical behavior on determining the fairness in prices involves the commitment with absolute norms in which the firms respect certain rights. As a consequence, new questions are raised about the rights themselves and the perception of unfairness in regard to the prices.

Fair price was described by Huppertz, Arenson and Evans (1978) as an "equitable distribution of the benefits" (p.251) from the exchange between companies and consumers, but according to Julio J. Rotemberg (2011), the distribution of benefits among stakeholders are difficult to define and measure, closely depending on industry characteristics and market power (p.7).

The pharmaceutical industry spins a complex ethical discussion as the commodity traded by them can be considered as priceless. When it is vital to save lives, it holds a particular non-market value and thus doesn't suit the commercial logic of trade. Additionally, the sellers have a strong market power as the concentration of vaccines is limited to a few big biopharma companies able to supply the global demand. Such context makes the question of fair price have a much greater importance. How would it be possible to ensure that a partner with a stronger negotiation power won't use such advantages to seek unethical profits? How would it be possible to have equitable distribution of the benefits for the weaker partner?

According to the World Health Organization (WHO) in the Market Information for Access to Vaccines (MI4A) released in December 2020, the global 2019 market value[1] for vaccines was estimated to be approximately $33 billion (WHO, 2020, p.1), which the European market was accounting as the second largest, estimated at USD 6.2 billion (19%), with an annual sale volume of 0.4 billion doses (WHT,2020, p.3-10). This billionaire industry has 80% of the world's revenue supplied by four large international companies called the "big four", consisting of the following: GSK, Merck, Pfizer and Sanofi (AMF, 2017, p.9). There are as well other few

[1] The primary data source is purchase and schedule data reported by countries through the WHO-UNICEF JRF, supplemented with additional publicly available information from PAHO RF, UNICEF and past WHO MI4A individual vaccine market studies. Remaining information gaps are filled using the Global Vaccine Market Model (GVMM), which estimates demand and price by country and vaccine across all WHO Member States, leveraging publicly available information.

companies growing in volume and are especially targeting developing countries, such as Serum Institute of India (the largest one in sales by volume), Microgen, and Johnson & Johnson (WHO,2018, p.4), with the potential to enhance vaccine accessibility.

Milton Friedman, an American economist of the Chicago School, argues that the drug companies can charge whatever price the free market accepts as the only social responsibility of a firm is to increase profit (as cited in Schlegelmilch,1997, pp.344-345). This view allows companies to charge up USD 540 for a infantile pneumonia vaccine (pneumococcal conjugate), as supply is limited by only two pharmaceutical corporations producing it (Pfizer and GSK); smaller countries with less negotiating power can often be compelled to pay more. Illustrating this situation: Lebanon pays about USD 243 against USD 189 paid by France for the same pneumonia vaccine. (Médecins Sans Frontières, 2019,para.3)

Discussing prices matter, especially when even a slight lower price could represent more doses purchased, hence more lives protected.

2.1 Health as a human right

The market power influencing the vaccine pricing plays a role in safeguarding the human right for health. Although some intellectuals defend that health should be seen as a regular commodity (for example: Thomas M. Gorrie, Ian Maitland and Mark J. Perry), it became undoubtedly a fundamental human right in the 20th Century. It was regulated by written norms to guarantee that each individual has the right to a complete state of physical, mental and social well-being, regardless of race, nationality, beliefs, and economic or social condition. It is only with health that the individuals are able to fully exercise the other fundamental rights.

The right to health was crystalized in 1948 through article 25 of the Universal Declaration of Human Rights (UDHR), stating that:

> "Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control." (UN, 2020)

Later in 2000, the right to health was absorbed by the Charter of Fundamental Rights of the European Union – document which catalyzed the fundamental rights of EU inhabitants – in its article 35, it was described as "the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices." (EU, 2020)

The EU statement is in line with the orientation from the committee responsible for monitoring the International Covenant on Economic, Social and Cultural Rights (CESCR) of the United

Nations, which understands that the entitlements of "health" include: "The right to a system of health protection providing equality of opportunity for everyone to enjoy the highest attainable level of health; The right to prevention, treatment and control of diseases; access to essential medicines." (UN, 2008)

Together with the legalization of the right to health started the awareness of the social, economic and political structures that underlines health. In other words, the right to health cannot be seen isolated, as it is multidimensional. Well-being is not only related to an individual's biological composition but also intrinsic, linked with the right to the enjoyment of a variety of goods and services (including the conditions necessary for accessing to them) and therefore socio-economic conditions.

Several studies already evidenced the role of lack of access of clean water and sanitation, income inequality, corruption and inefficient government downgrading the health levels of a country. The interconnection of all these circumstances might be an obvious conclusion nowadays, but the scientists go steps further to evidence how the burn on health is translated.

In 1993 Lant Pritchett and Lawrence Summers demonstrated in their article "Wealthier is Healthier" the causality between increase of per capita income and decrease in infant mortality: if in the developing countries income had been one percent higher in the 1980s, up to half a million childrens' lives would have been saved. According to the researchers, others factors besides rising income clearly participated in determining health. An example would be an efficient public program and higher status of women (Pritchett and Summers, 1993).

Therefore, the right to health needs to be operationalized by multiple agents, not only by the governments. It requires commitment among several stakeholders as civil society, academia, nongovernmental organizations, international institutions and corporations effectively deal with all the social and economic variables that impacts health. A wholesome population with longer life expectancy is more likely to invest effort and time in developing its human capital, which in time contributes to speed the creation of more advanced medicines and spread innovative technologies.

2.2 How fair price is perceived

The perception of fairness is not a straight way to be measured, especially when it touches on fundamental rights such as health. Consumers demand that companies demonstrate a minimum level of altruism to perceive a price as fair, according to Rotemberg's model (2011, p.4).

A common observation in academic studies focuses on the sensitivity on increasing and decreasing prices versus a reference price transaction. Kahneman, Knetsch and Thaler (1986, p.735) found out that respondents perceive as unfair when a company raises the prices when there is a sudden high demand.

In a study from Harvard Business School conducted by Julio Rotemberg (2011, pp.4-5), two main findings regarding the translation of the fair pricing experience were released: first, "consumers expect firms to be somewhat altruistic towards them and that they react with anger if firms prove to be insufficiently altruistic"; second, consumers experience a loss (or a regret) when they pay more for an object that could have been easily found at a lower price earlier.

It becomes easier to understand when illustrating Rotemberg's conclusions with the recent health crisis brought by the Covid-19 pandemic or the past swine flu pandemic, which caused a high demand on drugs to treat the symptoms but also a run to therapeutic drugs.

In the US, the drug companies did lobby vigorously to avoid having a price limit to Coronavirus treatments developed with federal emergency funding and they won based on the argument that government constraints on pricing would limit private investment. The repercussion was immediate. According to the Democratic congress woman Jan Schakowsky: "The idea that drug companies should have free reign to set prices during an international pandemic is immoral and dangerous."

Another statement on the same topic was made by the executive director of Social Security Works, Alex Lawson: "And at some point, people are going to start wondering why the federal government pays unreasonable prices on anything to pharmaceutical companies. And when that happens, that's when pharma's whole house of cards starts falling down." (Karlin, 2020).

In Europe, while the Covid-19 pandemic is still greatly impacting the continent, there was no discussion on the table about setting up a pricing rule on a new vaccine or drug to combat the Coronavirus until April 2020. It is an unfinished effort to have the EU countries cooperating on the health technology assessment (HTA) - a system through which the policymakers would be able to decide on how much to invest in public health for a new drug or treatment. As each member state is responsible for their own health services, it seemed that for now the European Union (EU) decided to adopt an approach focusing on coordinating the health crises measures between the Member-States instead of taking an active role discussing pricing to avoid add more tension on top of this sensitive juncture.

For the moment, it is not possible to entirely judge if the strategy of the EU to leave out the pricing discussion with a pandemic raging currently is the most assertive or not, but Europe already had experienced about a decade prior the H1N1 flu pandemic and how the lack of transparency can let the public health institutions more susceptible of the big pharma players - a lesson that was seemingly not fully absorbed by the politicians. Quoting the Parliamentary Assembly Council of Europe (PACE) on Resolution 1749/2010 about the handling of the H1N1 pandemic:

> "The Assembly notes that grave shortcomings have been identified regarding the transparency of decision-making processes relating to the pandemic which have generated concerns about the possible influence of the pharmaceutical industry on some

> of the major decisions relating to the pandemic. The Assembly fears that this lack of transparency and accountability will result in a drop in confidence in the advice given by major public health institutions. This may prove disastrous in the case of a next disease of pandemic scope, which may turn out to be much more severe than the H1N1 influenza." (PACE, 2010).

The organization Médecins Sans Frontières advised that high prices and monopolies can lead to the rationing of medicines, tests and vaccines, which in turn would prolong the Covid-19 pandemic (MSF, 2020). In any case, with or without a European regulation of price on a Coronavirus therapy before the discovery of a solution, one expected behavior of the population is the intolerance of an inaccessible price. The reactions can become not only angry but furious considering all the social and economic background of the worst modern pandemic ever seen.

The second finding of Rotemberg can also be experienced by consumers as they might pay more for the same drug during the effects of the Coronavirus outbreak when the stock of the drugs requires reloading. This increase in its price is not necessarily linked with the increase in the profit margin of drugs manufactured but most likely due to the increase of the cost of the ingredients if the pharma companies decide to not absorb the loss in their margins to keep the price level. It especially affects the generic drugs (e.g. Paracetamol), as they are frequently using low cost supply imported from India and China where the production was affected and changing to a new supplier is not easy due to the requirement of regulatory filings; it may bring additional unplanned costs or even disruption of the supply. In this case, the consumer's perception of fairness will be downgraded as they cannot be able to purchase the same drug with the previous price, feeling some loss or regret of not having had stockpiled with the prior lower price.

Coming back to the past, in June 2009 the WHO declared a new influenza virus (H1N1 or swine flu) as a pandemic and since April 2009 the organization had advised all countries to activate their outbreak preparation. In that time no vaccine was available (they were only approved by FDA and EMA in September 2009), but there were two antiviral drugs already in the market displayed as options by the Committee for Medicinal Products for Human Use (CHMP): oseltamivir (Tamiflu) and zanamivir (Relenza) (EMA, 2009a). Some countries decided to strategically stockpile, a measure which was considerably controversial between specialists, raising questions like the lack of strong scientific evidence base, cost–benefit of this strategy and hidden commercial interests. Researchers of University of Sussex estimated that 95 countries purchased or ordered pandemic Tamiflu from Roche to stockpile by 2009, without pricing transparency as most countries kept the price paid confidential, leading the estimation of cumulative costs on billions of euros across the EU member-states (Elbe, Roemer-Mahler, and Long, 2014). The pharmaceutical companies hold a central role in the pandemic preparedness, enhancing even more their market and influential power, but this did not pass by indifferent throughout society.

In response to the so-called “pandemic scandal” by the press the Council of Europe in 2010, an inquiry about the influence of the drug firms on the global H1N1flu campaign was opened, targeting the bias on WHO overrating the swine flu health crisis. The former chairman of the Health Committee of PACE (Parliamentary Assembly of the Council of Europe) and epidemiologist Wolfgang Wodarg stated that it was one of the greatest medicine scandals of the Century, in his own words:

> "(…) in order to promote their patented drugs and vaccines against flu, pharmaceutical companies influenced scientists and official agencies responsible for public health standards to alarm governments worldwide and make them squander tight health resources for inefficient vaccine strategies, and needlessly expose millions of healthy people to the risk of an unknown amount of side-effects of insufficiently-tested vaccines." (Sturcke & Bowcott, 2010).

The inquiry resulted in the edition of the CAPE Resolution 1749/2010, concluding with the European Assembly inviting the pharmaceutical corporations to revise their co-operation functioning with the public health topics to ensure higher transparency and corporate social responsibility (CAPE, 2010). It seems that not only the consumers are expecting from a certain level of altruism (Rotermberg, 2011, p.4) from pharma companies, as Rotermberg found in the prementioned research, but also the governments.

An example of intense society reaction regarding fairness on pricing deserves mention. In 2019 a Belgian baby was born with spinal muscular atrophy (SMA) and an innovative drug able to cure it, produced by Novartis (Zolgensma), cost about 2 million euros, making it the most expensive therapy ever produced. As Zolgensma was not fully accessed by the EMA, it was not covered by Belgian health insurance. Society pushed for the Health Minister, Maggie De Block, whose called the responsibility to the drug maker stating: “It's very cynical to see that some companies consider society as nothing more than a cash cow” (Politico, 2019). Novartis, in turn, justified its high price by comparing it with a potential offset/saving of not using a life-time treatment (Spinraza) versus their one-shot treatment.

The fairness or unfairness of a therapy price is definitely not an easy object to be quantified and analyzed but becomes more sensitive when identifying society’s reactions when the prices are disruptive or during a pandemic. The current classification as a pandemic of Covid-19 could be reverted to an epidemic by WHO within 2021, consequently prices will potentially become higher with manufacturers charging with profit margins (instead of the exceptional cost of production). If so, can be expected that discussions regarding price sensitiveness become more present and consumer might eventually perceive prices as less fair.

2.3. How to have an equal distribution of benefits

The discussion regarding price and the distribution of the trade benefits between consumer/governments and vaccine providers tries to dismount the complex ethical dilemma.

There are several lines of thinking under ethics linked with theories of justice that are able to provide this answer, depending on what will be the concept of right or good adopted to promote fairness.

It is not a contemporary topic, as its roots can be recalled in Aristotle's conception of justice in 4th century B.C. According to Aristotle the price formation should be set at a level to keep the initial social order identical after the transaction. In other words, the price should be proportional to reflect the relative status of buyer and seller; if the buyer is poorer than the seller before the trade, after the transaction the buyer should be exactly as poor as he was before the trade. (Jorion, 2015) By his theory, it can be extracted the idea of avoiding disproportional gains by one of the trade stakeholders, which would be used as an ideological base for other philosophers later.

In topics related to health, the ethical theories commonly present in the writings are utilitarianism and libertarianism, as in both theories a normative aspect is taken on, focusing on best outcomes and efficiency.

Headed by John Stuart Mill and Jeremy Bentham, utilitarianism is a well-known example of consequentialist theory since the judgement of whether an action is right or wrong is only assessed by its consequences. The utilitarian approach seeks activities which can result in the maximal utility (which does the most good and the least harm) for the greatest number of people. For this reason, it suits the vaccination policies at a certain instance because vaccines are a preventive treatment that benefits a high number of people with relative low investment in a short run. Although it is important to have in mind that the utilitarian theory doesn't justify the investment for all types of vaccines like the ones that target long runs (ex. pandemic flu), to prevent infrequent diseases (ex. zica, dengue) or for a specific niche of the population (ex. HPV for adolescents, Shingles for elderly). In other words, under utilitarianism theory, it would be acceptable to allocate resources in vaccines if they are cheaper than other alternatives and if they are suitable for the majority of a population universally for a common disease. This ideology doesn't properly answer the question of equal distribution of the benefits for the weaker stakeholder as it does not respect the person who holds them and neither considers its utility axis (the ability to pay or basis of need), but instead aims to make things better for everyone collectively.

In the other extreme, contrasting to the utilitarian theory and considering that people shouldn't be used solely as means to the welfare of others due the violation of the fundamental right of self-ownership (Sandel, 2009), libertarianism defends the individual's freedom of choice (not the government or anyone else) to determine what is right or good for themselves. The exponent of libertarianism theory was John Stuart Mill, defendant of an unfettered market not only as a way to maximize welfare but an important way to exercise the right of liberty by free pricing between buyers and sellers according to factors of demand and supply. Thus, it seems that libertarianism is the most suitable ethical theory from the industry's perspective since it implies freedom for the manufacturers to allocate investments and sales driven by its greatest profits.

Ultimately, the problem with libertarianism theory is that it ignores the people victimized by this free market system. There must be limits to business morality when its chooses to seek high profit under the cost of harming people's health because these people cannot afford a vaccine due the greed of greatest dividends. For libertarians, the weaker part on the trade relation- the consumer- is not better off, the purchase of vaccines is an individual matter, the free-market auto regulates the price and therefore, the access to vaccines is an individual issue, not a social responsibility. It consequently omits the individuals that do not have their own means to purchase the treatment.

A theory of justice proposed by Harvard professor of political philosophy and ethics, John Rawls, might address better the problem of the distribution of benefits related to topics of health. Rawls understands fairness as the fundamental idea in the concept of justice (Rawls, 1958).

According to Rawls, to assess justice, it is necessary to ask what the principles should be agreed upon in an initial situation under an independent standard of fairness – the "veil of ignorance". Or in other words, what would be the common moral determination of the social contract, without knowing your and the counterpart's gender, class, race, ethnicity, level of wealth, and education for example. So, under the "veil of ignorance", he believes people would adopt a system of equal basic liberties for all citizens. The inequalities in opportunity and income would be accepted only when this bias works to the benefit of the least advantaged members of society- this is called Rawls difference principle. (Sandel, 2009, p. 152)

Since these inequalities are most likely present in society, to establish fairness it is necessary to treat differently the unequal individuals to obtain fairness. Contextualizing with an example of such acceptable inequality would be if prices of vaccines were cheaper or free for the poorest individuals or countries. This given example matches the notions of fairness developed by Rawls' theory of social justice and entails equality of both means (opportunity) and outcome (consequence).

However, the same theory could be elaborated to justify the inequalities in the other direction, accentuating the relative inequality under the excuse to promote a general equality. For example, a vaccine company could argue its price disparity facilitates product competition amongst the industry or investment in R&D to the degree that it results in improvements in vaccines standards or the development of new products that raise the general quality of vaccines. In any case, the major precondition for this healthy competition would be that the citizens are well informed, understanding properly the pricing differences and standards between companies. Then, the implementation or adoption of a value-based competition, whereby unrestricted competition based on results promotes an increase in value for patients, according to the economist Michael Porter (as cited in Pentecost, 2006).

Some researchers like David Resnik, Normal Daniels and Dan W. Brock sustain that as long as the consumer (the least advantaged stakeholder) follows the current norm that is established, as example, respecting the intellectual property rights, the pharmaceutical companies have the social responsibility to supply the therapies to the impoverished. For the researchers, however, this help needs to be limited by contingencies and thresholds on the requirement (Engelhardt & Garrett, 2008, p. 47).

On health matter intent and consequence of the actions to promote fairness, essentially to ensure the achievement for the most vulnerable and odd ones in a long run, not only by the ones able to afford vaccination or the maximum universal number of people. A fair price to pay for a vaccine would be the one setup at a such level able to promote the equality of access to all citizens, safeguarding the right of health to all. Only when the individuals can dispose of a good physical condition, they will be able to enjoy the others normal range of rights afforded in a free society. For this goal to be reached it must balance the divergences that invariably may occur along the way, and the greatest challenge will be to find the common denominators under the “veil of ignorance”, the ones which respect moral principles but can also be applicable for political and economic interests.

3. European Health System for Vaccination

The EU health system through its national government or centralized EU institutions have a key role on the structure, conduct and performance of vaccines in Europe, not only for being the agent that setups policies but also because it is the main source of demand. The vaccines for robust immunization programs are generally purchased by governments directly or through some pooled-procurement system (AMF, 2017, p.9) and it is the own country that decides which vaccines will be available (mandatory, recommended and/or reimbursed). This multidimensional public role reverberates in the dynamics of the vaccine innovation through a potential unequal incentive of vaccines development focused on diseases of high-income countries and overall price fairness (Bessa, 2017, p. 2).

The first important concepts to have in mind are vaccine and immunization. Vaccine is a biological preparation that stimulates body immunity to a fight against an infectious agent through the antigens (mostly weakened or killed forms of a disease-causing microorganism). Once the vaccine harnesses the natural activity of the immune system it can more easily recognize and destroy any of these microorganisms in later encounters promoting the immunization thus protecting against a disease (WHO, 2016).

A high level of immunization coverage of the population is essential since vaccination protects individuals and also those who have not been vaccinated by breaking the chain of transmission, making possible the avoidance of epidemics or pandemics - situation called by herd immunity when sufficient proportion of the population is vaccinated it is less likely that the disease will spread (WHO, 2008).

Through the recent Covid-19 pandemic in 2020, the entire world was able to recognize the importance of vaccines, experiencing all the negative effects of not having one in place and how it can impact our daily routines, endanger risky population groups, increase mortality, jeopardize the economy - and all these consequences are not even scratching the surface of much deeper issues caused by a pandemic.

Viruses and diseases do not respect national borders. From an institutional level it was evident to the European Commission (EU) through the Directorate-General for Health and Food Safety (DGHFS) that they should have ensured more affordable and accessible supply while supporting sustainable innovation on research and clinical trials (EHFG, 2020). But the 27 European Union countries have been built by different cultural heritages, developed by particular histories and interests that shaped their health care systems as it is today (EP, 1998, p.5-6).

Gradually the countries have been committing to improve health for all citizens, reduce the health divide and strengthen governance for health with for example the adoption of common assessment tools such as health technology assessments (HTA), channels for centralizing purchases and agreeing upon the WHO European policy framework for Health 2020. To

converge all local diversity into a common vaccine framework seems to be a huge challenge for the European institutions.

3.1. Framework of health system in Europe

The EU structure of the health system varies considerably between and within each member state, often caused by the differences in the constitutional organization levels (national or local/regional) which provoke ramifications of power and responsibility from legislation to policy development, implementation and funding. While the EU can sometimes reach a consensus regarding the core components of the health strategy for the entire block, there is a need to better understand how it can be effectively integrated when cascading at country level and translating to effective health rights.

The framework of the European health system is primarily national, and each Member State holds the initial responsibility to organize and deliver health services and medical care in its territory. The EU serves secondarily or as a subsidiary, complementing national policies, supporting and coordinating actions, adopting binding specific legislation (e.g. medicines, clinical trials and medical devices), providing tools to promote cooperation, and helping national systems operate more effectively (EU Health Policy, 2021).

In other words, the EU has limited legislative power in the field of human health due to absence of a clear legal basis (EP, 2021, para 7). According to Anniek de Ruijter it was a result of Member States' resistance to transferring major powers to to EU because "that health services form the centre of nation states' welfare provisions, and in most EU Member States health spending is one of the largest single chunks of the national social welfare budget". (Ruijter, 2019, para17)

Although the responsibility to protect and promote human health remains legally under accountability of Member States, some authors as Ruijter, McKee, Greer defend a crescent role of the EU power. This increase of EU influence can be illustrated though policymaking, setup of supra national agencies such as the European Medicines Agency (EMA), the European Centre for Disease Prevention and Control (ECDC) and Executive Agency for Health and Consumers (EAHC), and even ruling on topics that impacts health such as food, environment and response on major health threats (e.g. bioterrorism and epidemic) (EP,2021).

Under the scope of response to health threats, in 2014 the EU approved a Joint Procurement Agreement (JPA) which enabled Member-States, EEA and more 8 countries to procure pandemic vaccines as a group, at more balanced prices, ensuring equal treatment and committing a high level of solidarity between members (EC-PH, 2021, para 11-15). No straight information regarding any public disclosure of pricing is stated. The JPA was created in the context of Flu H1N1 Pandemic of 2009 responsiveness and no transparency on the costs were shared on the allegation of confidentiality due to intellectual property rights and trade secrets (EC, 2019, para 32-33).

Another mechanism utilized by the EU under its health prerogative was the introduction of the HTA in 2013 to improve the transparency of health care data and encourage innovation by rewarding high added value technologies between the Member States. It is a tool that measures the added value of a new health technology compared to existing ones though disclosure of information about the formulation of safety, effectiveness, cost and economic evaluation.

HTA is providing policymakers and lawmakers insights to discuss health topics supported by database evidence, as well as helping national authorities in decisions of which technology to reimburse at country level. Nevertheless, HTA missed a great opportunity to further improve transparency, including pricing and reimbursement criteria in its database, which was not done under the prerogative that it is a national subject (Natsis, 2018, pp3-4).

Regarding the funding of the European health system, it can be private when the funding from voluntary insurance schemes or public when tax-financed by means of fiscal tools (EU, 2012, p 100-101). In a nutshell, public funding is predominant in Europe (Thomson, 2009, p.25) and can be funded by general tax on revenues or/and through compulsory social security contributions, usually by employers and employees. These economic aspects of funding health through solidarity principals are fundamental to ensure accessibility of vaccines to all society.

This model of funding is a target of criticism due to its fragility when health demand increases, making public spending with health services higher than respective increase in the gross domestic product (GDP) to finance it. To balance the right for health and ensure social protection while the sources of revenues are constrained is a frequent challenge for countries.

In order to provide an idea of the magnitude of health care expenditure in EU countries is essential to illustrate with data. It represents approximately 10% of the EU GDP (EC, 2015). Projecting it with 2019 EU GDP the cost with health would represent about 1.6 trillion dollars (IMC, 2021), not considering the scenario of additional costs caused by the Covid-19 pandemic.

In such context of raising public expenditure with health care, some decades after World War II, around 1980, the European Nationals policymakers drove efforts on cost-containment measures in health which most of the time was not considering the people-centric approach (Carone *et al*, 2012, p.5). Such background reflected in the prior drivers of European Commission healthy security framework which based on three pillars: prevention, preparedness and responses to threats.

Recently the focus started to shift to a sustainable model with emphasis on the return on investment, improved patient-relevant outcomes and the population's health. Current policies and actions in European public health are offering more granularity and targeting in patient-centric approach translated in three goals: a) Protect and improve the health of EU citizen; b) Support the modernisation of health infrastructure; and c) Improve the efficiency of Europe's health systems (EC, 2020). In other words, these objectives can be translated from a patient's

perspective as better and accessible services, more power to choose their treatments and providers (EXPH, 2015, p. 15-17).

However, public economists are still struggling to balance the financial equation for funding health expenditures without reviewing the scope of (universal) health coverage in a context of economic pressure, rising health care costs and changing disease profiles of ageing populations. One path for the solution is by investment in well-being and promotion of healthy ways of life (e.g. tackling smoking, alcohol abuse, obesity and physical inactivity), therapeutic and preventive medical solutions to avoid spread of communicable diseases, further complications triggering more expensive or longer treatments (EU,2019 and Dyakova *et al*, 2017). It seems that vaccination can play a role in safeguarding public budget.

3.2. Vaccine program in Europe

Immunization through vaccine have been considered as one of the main cost-effective public health strategies to prevent, control, and eradicate several communicable diseases (Bessa, 2017, p. 1). It would therefore be expected that European nations and EU policies perform an active role to support vaccination program accessibility and R&D innovation for further diseases.

The vaccination programs in all EU Member-States are organized at the national level, whereas the regional level plays a role in overseeing implementation and monitoring vaccination coverage. Only in few countries the regional level has autonomy to customize the national vaccination programs to local needs like in Germany and Spain (Rechel *et al*, 2018, p. 11).

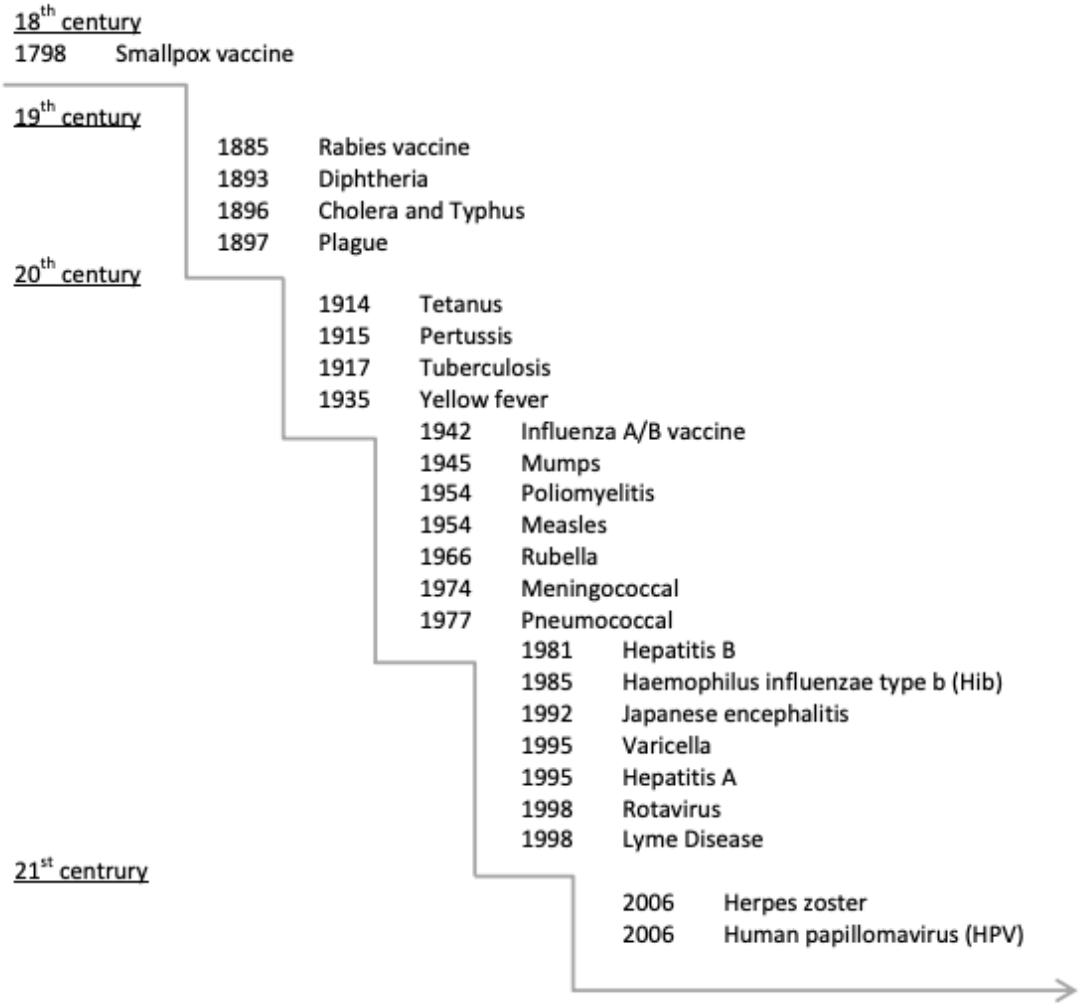
Health care always has been in the center of tensions between EU central directives and Member-States, but one of the major conflicts centered around vaccination. In 2018 when measles cases were extremely high in Europe, the countries still hesitated to give to EU more power over vaccination programs (Jennings, 2018, para. 8). Only recently a path to study the feasibility to align the national vaccination schedules by 2020 started but the final recommendation of the Health Council was not successful. It may be the necessary push caused by Covid-19 to increase the awareness of vaccination and mobilize politicians to align with a broader and uniform vaccination program within the EU.

The EU was assertive when it decided to prioritize policies for health 5 years ago. Promoting vaccination has been included as one of the six main items to be achieved in the Strategic Plan 2016-2020 of the Commission's Directorate-General for Health and Food Safety (EU Health Policies, 2020).

The availability of different vaccines has increased in the last decades, one part from a common package used to immunize children (e.g. measles, poliomyelitis) and other parts given to particular groups, such as travellers (e.g. yellow fever or cholera) or those at occupational risk (e.g. rabies) (Rechel *et al*, 2018, p.10). From the 18th century, with the introduction of the smallpox vaccine to nowadays with the newest coronavirus Covid-19 vaccine, there were at

least 26 vaccine-preventable diseases available in Europe. The number of vaccines in the market is constantly changing, with new products being added to national schedules or being removed because the disease no longer exists or the vaccine has limited effectiveness as in the example of smallpox or paratyphoid A/B.

Figure 3.2. 1 *Historical timelines of vaccine development*



Note. The timelines of vaccination Programs in Europe from 18th century to 21st century. Reprinted from Expert Panel on effective ways of investing in Health (EXPH), Preliminary report on Vaccination Programmes and Health Systems in Europe, 26 September 2018, p.12. Copyright 2018 by European Union. Reprinted with permission.

It was only after World War II that the immunity agenda through vaccination turned into a comprehensive policy spread across countries, progressing quickly in the 70s and 80s. (Stevens, 2007, p.220) Although it seems remarkable for humankind, the EU is still facing increasing outbreaks of vaccines for preventable diseases, reporting fatal cases of measles and diphtheria and managing the rise the vaccination avoidance in society (EC,2018, para 6).

As same as the framework of other health solutions across the block, the vaccination program is not homogeneous, as it varies according to the national legislation. In some countries it can be mandatory and in others recommended depending on the population groups like infants or older adults for example. If mandatory, on one hand it can become unpopular with some individuals but on the other hand it might be essential to achieve a herd immunization of the population. Remaining challenges on the regional and national level still need to be addressed to assure improvements towards the objective of promoting the vaccination within the European Union.

To illustrate this heterogeneity in 2018, the EU released the expert panel regarding to the effective ways of investing in Health, a survey done in 2010 about mandatory and recommended vaccines in children with 29 countries in Europe including the EU, UK, Iceland and Norway: all countries included 8 vaccinations against diphtheria, hepatitis B, Hib (haemophilus influenza b), influenza, MMR (measles, mumps, rubella), pertussis, polio, and tetanus in their programs as either mandatory, recommended or reimbursed (EU, 2018, pp 43-44).

For the mandatory vaccination, only 48% of the countries (14 countries) had at least one mandatory vaccine: as example the polio vaccine is mandatory for both children and adults in 12 countries, diphtheria and tetanus vaccination was mandatory in 11 countries, and Hep B in 10 countries.

On the contrary, analysis of 15 countries that don't have mandatory vaccination (such as the Netherlands, Luxembourg and Germany) showed that just with recommended vaccination programs, these countries seemed to achieve equal or better coverage rates as countries with mandatory programs like Italy and France vaccinations (Havarkate *et al*, 2012).

The correlation between increase of a country's protection against a disease and the compulsoriness of the respective vaccination is still not fully studied but great academic discussions regarding justice, autonomy and benefits in specific groups were covered (Galanakis *et al*, 2013; Hendrix *et al*, 2016; Navin *et al*, 2017).

Figure 3.2. 2 *Mandatory and Recommended vaccines for children in Europe in 2010*

A Country	Diphtheria	*Haemophilus influenzae* type B	Hepatitis A	Hepatitis B	Human papillomavirus[a]	Influenza	Invasive disease caused by *Neisseria meningitides* group C
Austria	RA	RA	RR	RA	R	RR	RA
Belgium	RA	RA	RR	MR/RA[b])	R	RR	RA
Bulgaria	MA	MA	RR	MA	R	RR	A
Cyprus	RA	RA	RR	RA	A	RR	RA
Czech Republic	MA	MA	MR	MA	R	RR	RR
Denmark	RA	RA	RR	RR	R	RR	RR
Estonia [6]	RA	RA	RA[e]	RA	R[e]	RA[e]	RR[e]
Finland	RA	RA	RR	RR	A	RA	A
France	MA/MR/RA[f]	RA	RR	MR/RA[b]	R	RR	RA
Germany [7]	RA	RA	RR	RA	R	RR	RA
Greece	MA	RA	RA	MA[h]	R	RR	RA
Hungary	MA	MA	MR	MA	A	RR	A
Iceland	RA	RA	RR	RR	A	RR	RA
Ireland	RA	RA	RR	RA	R	RR	RA
Italy	MA[l]	RA	A[l]	MA	R	RR	RA/RR[k]
Latvia	MA	MA	RR	MA	MA	RR	RR
Lithuania	RA	RA	RR	RA	A	RR	RR
Luxembourg [8]	RA	RA	RR	RA	R	RR	RA
Malta	MA	RA	RR	RA	A	RA	A
The Netherlands [9]	RA	RA	RR	RR	R	RR	RA
Norway	RA	RA	A	RR	R	RR	A
Poland	MA	MA	RR	MA	R	RR	RR
Portugal	RA/MR	RA	A	RA	R	RR	RA
Romania	MA	MA	RR	MA	R	RR	A
Slovakia	MA	MA	MR/RR[p]	MA	R	MR/RR[o]	RR
Slovenia	MA	MA	RR	MA	R	RR	RR
Spain	RA	RA	RR/RA[k]	RA	R	RR	RA
Sweden	RA	RA	A	RR	R	RR	A
United Kingdom	RA	RA	RR	RR	R	RR	RA

A: absence of recommendation, MA: mandatory for all; MR: mandatory for people at risk; R: recommended; RA: recommended for all; RR: recommended for people at risk.

[b] Mandatory for healthcare workers.
[d] RA: conjugated vaccine to children younger than two years of age.
RR: polysaccharide vaccine to older persons.
[e] Not included in the national immunisation programme, but recommended by the Ministry of Social Affairs [10].
[f] MA: children up to 18 months of age.
MR: healthcare workers.
RA: bolder than 13 years of age.
[g] MA: children up to 13 years of age.
MR: healthcare workers.
RA: older than 13 years of age.
[h] No penalty exists for non-compliance.
[l] One of 20 regions does not have any mandatory vaccination as of 2008.
[k] Regional variability.
[m] Rubella: mandatory for girls by the age of 14.

Note. Modality of implementation of childhood vaccination program by country, the Europe Union countries, UK, Iceland and Norway in 2010. Reprinted from Expert Panel on effective ways of investing in Health (EXPH), Preliminary report on Vaccination Programmes and Health Systems in Europe, 26 September 2018, p.46. Copyright 2018 by European Union. Reprinted with permission.

The presented overview displayed in figure 3.2.2 can provide us a glance of the complexity for EU to build up a similar policy across all Member States for childhood vaccination as health programs are under the national framework. Such heterogeneity and use of own national procurement system to purchase vaccine don't contribute to improve transparency in pricing as information is not consolidated or shared between the Member States and represent a waste of opportunity to negotiate better prices using the volume as a bargain factor if purchased collectively for the entire block.

Furthermore, the economic burden on the individuals or family when paying for a vaccine could represent an obstacle for the engagement with this type of immunization program, bringing vaccination coverage even to lower levels. Illustrating with the findings on a 2018 report prepared by the European Observatory on Health Systems and Policies, the existence of out-of-pocket payments was considered as a barrier by 9 Member-States to higher coverage rates of Influenza vaccine in adults (Rechel *et al*, 2018, p. 12-13), which 7 Member-States (Austria, Belgium, Bulgaria, Estonia, Latvia, Poland and Slovenia) the targeted adult patients need to pay at least part of the costs.

Thus, for a better outcome of immunization coverage the prices of a vaccine would be reduced as low as possible for the patient or administrative barriers would be removed for them to get reimbursed, be completely publicly funded and/or combined with conditional access on public services (like school enrollment and social income programs).

To corroborate this view, a systematic review and meta-analysis conducted in 2013 by Diego Bassani *et al*. shared indicators suggesting that conditional transfer programs (such as financial incentives which would provide conditions for children to have access to preventive healthcare) may increase coverage of full age-appropriate vaccinations (Bassani *et al*, 2013, para 32).

Currently, the EU countries have blended different sorts of sanctions and incentives to improve vaccination coverage which includes awareness campaigns, financial rewards for health care providers or parents, and financial sanctions or barring access to school or kindergarten for those who refuse mandatory or even voluntary vaccinations (Rechel *et al*, 2018, p.11).

In order to promote an efficient and harmonized vaccination program in EU will be required a robust database to assess the target population and monitor results of vaccination; public procurement and the distribution agenda needs to be synchronized to avoid shortages, especially in the main season of diseases; and a sustainable public control on approvals for new vaccines and surveillance of safety and effective vaccine data to increase the trust of society.

While these challenges affect Member States in different ways, EU as a coordinator partner need to act to turn political visions into effective operational vaccination plans at national and EU level. Diseases are not bound by national borders, as only one Member State's weak immunization would put at risk the health and security of all citizens across the EU.

3.3 The influence of EU health system on vaccine market

The European health care framework, including its legislative system (national and central) and funding mechanisms, play a role in shaping the vaccine market and the prices. The vaccination, besides being an individual decision on be or not, is also influenced by the design and operation of health systems (Rechel *et al*, 2018, p.10). The policies and regulations bearing on current prices paid for vaccines can influence the new investments as it affects the firms' expectations for profits from future vaccines under development (McGuire, 2003, p.210).

Corroborating with this broad view, in the conclusion of a report made by Bernd Rechel and Martin McKee to European Commission in 2018 the authors mentioned that:

> "Thus, it is important that the administration of vaccines to individuals should not be viewed in isolation but rather should be looked at within a wider perspective that includes legislative frameworks, governance arrangements, accuracy and completeness of registers of target populations, funding mechanisms, and monitoring systems." (Rechel *et al*, 2018, p. 48)

The vaccine market is concentrated on both the supply and demand sides, and it is highly regulated and largely dependent on public purchasers and donor policies (WHO, 2021, para 1).

As so, it is important to understand how the EU Member-States, that are the agent of the vaccine regulation and also the main source of demand, influenced the market dynamics and firm's behavior using the support of the SCP (structure–conduct–performance) paradigm- analytical approach developed by Bain and Mason, among others (Lipczynski *et al*., 2005, p.6).

The SCP paradigm suggests an interconnection of links between the government policies on the structure of the market (ex: number, size and distribution of buyers and sellers; entry and exit conditions), which determines the firms' conduct (their competitive behaviour, such as pricing and R&D), which in it turn leads to the firms' performance (ex: quality delivered, profitability, efficiency) (Lipczynski *et al*., 2017, p.7).

Due the extreme regulation of markets by different policies either centrally in EU or nationally, only a few vaccine manufactures are able to meet the standards of quality established by the regulatory authorities. According to WHO, many of the individual vaccine markets are monopolies or oligopolies, either by product or presentation (WHO, 2021). In line with the SCP paradigm, it may be possible to accept an imperfect market structure such as a monopoly if its performance is consistent with an acceptable standard according to Clark (as cited in Lipczynski *et al*., 2017, p.6).

In order to explanation the causes of the industry concentration, it is worth to quote the findings of Institute of Medicine US Committee in 2003, although it is a research for the US specifically it clarifies the international context for biopharmaceutical industry also applicable for Europe.

The study found that a change in the US vaccine market dropped the number of suppliers from the 1960s through to the early 1980s, driven by 3 major factors, the first related to regulation, which follows:

> "(1) new FDA regulations, starting in 1972, that required evaluation of all previously licensed biological products (rather than submit data for evaluation, many firms simply withdrew from the market and requested that FDA revoke their licenses "without prejudice"); (2) growing concerns about liability; and (3) poor returns on investments relative to pharmaceutical and other products in the corporate portfolio" (IMC, 2003, p. 121).

According to the mentioned research, the changing structure of the US vaccine industry reflects an international trend of the declining number of vaccine manufacturers as a whole. Previously, the vaccine markets had regional (not global) leaders, with Pasteur-Merieux and SmithKline leading the European market, Merck and Lederle-Praxis in the US market, and three Japanese firms (Takeda, Eisai, and the Research Foundation of Osaka University) were the major suppliers for the Japanese market (IMC, 2003, p. 124). By the 1990s, global acquisitions, mergers, and joint ventures had reshaped the industry as a whole (Mowery and Mitchell, 1995).

This market dynamic currently concentrated on a few multinational manufacturers and raised concerns about potential disruptions of vaccine products, incentivisation of investigating new immunizing agents, and the exercising of market power by the firms.

The entrance of new supplies would potentially increase the fairness on price driven by more competition. According to WHO, the entry of emerging market producers, particularly in the underused vaccines market, has resulted in lower vaccine prices due to increased competition and higher production capacities for individual vaccines (WHO, 2021, para 3). But the vaccine industry has particular features which increase the complexity for new entrants, as well as the investment in R&D and the progress of vaccine technologies.

Therefore, it seems that the EU and Member-States have a strategic role in the vaccine market, whether being the agent that promotes directives, regulates the market, decides which vaccines will be available (mandatory, recommender and/or reimbursed) for its population or being the main purchaser of it. A more comprehensive overview of the interconnections of vaccine market agents will be explored in a further chapter, helping to illustrate how the EU regulatory policies along the entire chain of a vaccine development contributes as a barrier for new suppliers. The limited number of vaccine suppliers and production capacities leads to a tenuous balance between demand and supply in vaccine markets and so aggregates elements to jeopardize the fair pricing of immunizing products.

4.The cycle of a vaccine: from R&D to final user – pricing elements

What are the goods that you'll be able to list that took 15 years to be available for your use? The availability of a vaccine is complex, from the initial idea to finally administering the dose, and it is reflected in its high prices.

Historically, the first vaccines were introduced in an environment of unsanitary conditions and poor population health by the incidence and morbidity caused by infectious diseases, setting the high cost standard. However, nowadays the health environment has improved, and the vaccines can target other diseases such as cancers. Thus, compared with older vaccine technologies, the new ones may be more costly as a result of more advanced, complex, and patent-protected technologies (e.g., adjuvants, mRNA, recombination techniques and carrier proteins) as well as due to increased regulatory oversight (Rémy *et al*, 2015, p.4).

The research, development and production of a vaccine have been lengthy, bureaucratic and expensive. It is important to understand comprehensively the cycle of a vaccine due to the fact that often longer, riskier and more complex vaccines trigger higher prices, which in turn have a direct impact on its accessibility to society (Bessa *et al*, 2017, p.2).

As a vaccine is made by biological materials, it is harder to reproduce in large scale and they are under more regulation than traditional pharmaceutical drugs made by inert chemicals. For instance, before 2020, with the Covid-19 mRNA vaccine available in a record time of only one year, the quickest development for vaccine was for measles, which took 10 years to develop - the disease agent was discovered in 1953 and the vaccine was licensed in 1963 within the USA (Our World Data, 2021). Some diseases that have been around for a long time still don't have a significantly high efficacy vaccine, such as Malaria, one of the most communicable diseases in the world that is challenging the scientific community for over a century.

The whole process for a vaccine candidate to be approved and to be sold can take approximately 8 to 15 years in a normal vaccine timeline (Felter, 2021, para 19) because each candidate must be evaluated for safety, immunogenicity and efficacy in humans for a due region or country before it obtains approval.

Additionally, it is a risky investment because the majority of vaccine candidates fail. A driving factor for decision by researchers and investors to pursue an antigen investigation for a future vaccine is that the probability of success (PoS) of a clinical trial to become a safe and viable commercialized product. To estimate the PoS is not a straightforward exercise as it is required to gather accurate information on trial characteristics and outcomes, which is time-consuming, susceptible to error, and costly.

The complex vaccine cycle makes it so that investment on a new candidate is not as attractive for a great number of private investors as it would be in industries with higher profit margins and less complicated and shorter processes like clothing, beverage, raw materials or even

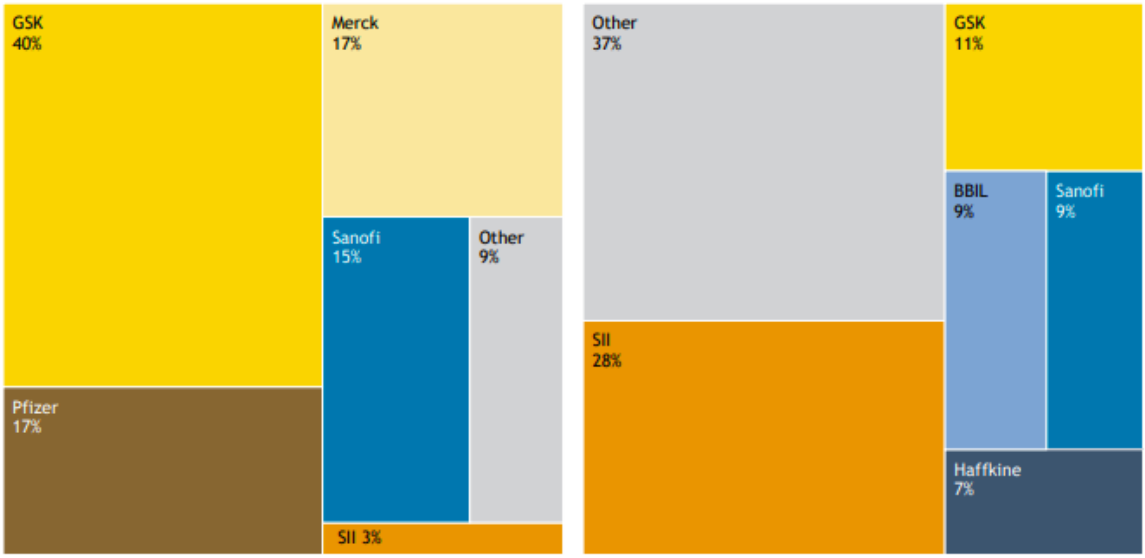
automobiles. It is an expensive investment, as the vaccine's R&D costs – essential for a vaccine product – range from 200 to 500 millions of dollars per successful product launch including sunk costs for failures. Creating a manufacturing facility could cost additionally from 500 million to 1.5 billion dollars according to David Bloom (Bloom *et al.*, 2020, p.55).

The structure of the vaccine industry, because of the aforementioned entry barriers, made the quantity and size of the manufacturers concentrated in a few multinational companies. Supporting this statement is a conclusion of Dr. Rudi Daems (2008):

> "Only a handful of pharmaceutical firms and several smaller biotech companies have historically developed the necessary drugs and vaccines for the protection and treatment of infectious disease. Basic scientific advances often occur in university research laboratories, but these public institutions are generally unable to spend the large sums of money that are required to transform the fundamental scientific discoveries into safe and effective prophylactic vaccine or drug treatments that can be approved and licensed. The transition from the initial medical-scientific discovery phase to the applied product-oriented development phase is more likely to occur in pharmaceutical and biotech corporations. They have the financial capacity and the technological know-how, combined with the human resources specialized in clinical testing, regulatory affairs, as well as engineering and manufacturing." (p. 4).

Illustrating with global perspective of the market concentration by two different views, from value and from volume:

Figure 4. 1 *Manufacturer share by global vaccine price (left) and volume (right) in 2019*



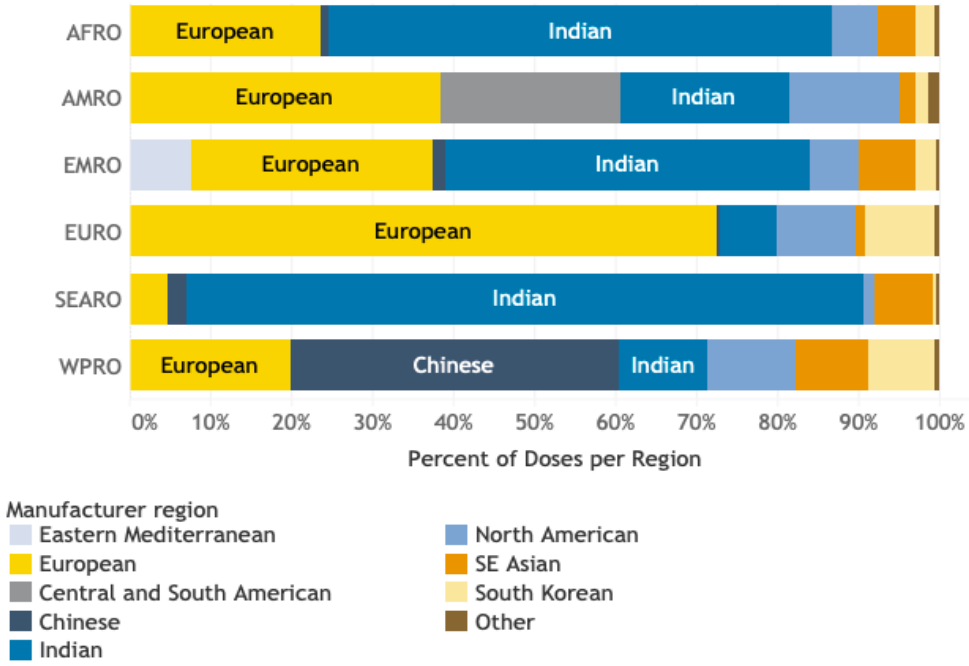
Note. WHO launched MI4A (Market Information for Access to Vaccines) in January 2018 in response to calls by the World Health Assembly, Member States and WHO's Strategic

Advisory Group (SAGE) on Immunization, which one of the goals is to improve access to market information for health commodities. Graphics inform about the vaccine market from the price and volume perspective in 2019. Reprinted from *MI4A Plataform*. Retrieved on March 20th, 2021, p. 4, from https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1#:~:text=MI4A%20estimates%20global%202019%20market,for%2068%25%20of%20global%20value. Copyright 2021 by WHO. Reprinted with permission.

It is visually clear in figure 4.1 that 90% of global vaccine value is controlled by four large firms (GSK, Pfizer, Merck and Sanofi), while by global volume 60% is supplied by 5 main companies (SII, GSK, Sanofi, BBIL and Haffkine).

Accordingly, this concentration of suppliers is reflecting in the number of prequalified vendors, the WHO disclosed that the majority of the vaccines (36) have two or fewer prequalified suppliers. The range of choice could be even more restrictive if considers the countries' preferences, for instance European countries rather buy from domestic or regional manufacturers, potentially because of regulatory[2] limitations, as well as political constraints (WHO, 2020, p.4), evidence confirmed by the figure 4.2.. Such scenario of lower competition (regional or global) plays a role in pricing.

Figure 4. 2 *Regional vaccine procurement by manufacturer location in 2019*



[2] Examples of regulatory requirements at country level which could represent a barrier for entry are: market authorization fee policies, dossier review timing and requirements, local language and product representation requirements.

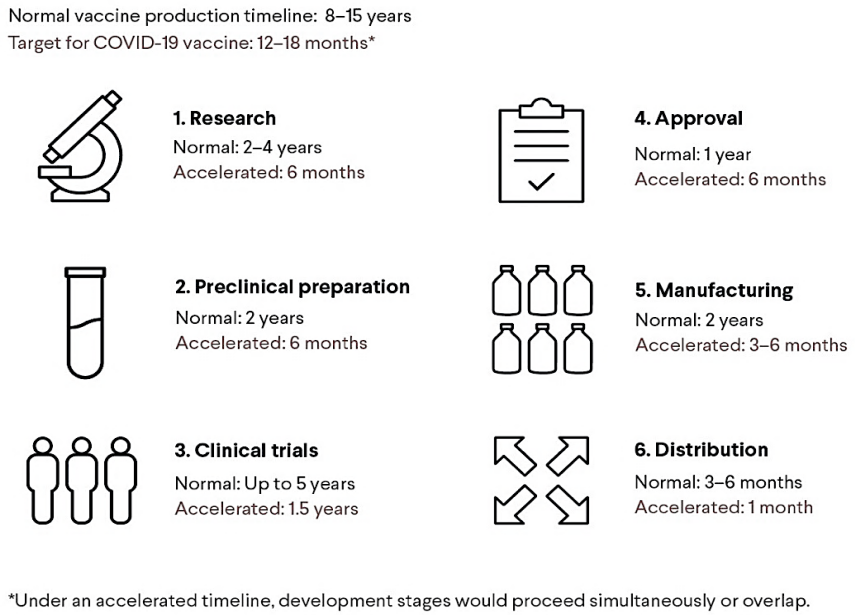
Note. Vaccine's market distribution by manufacturer location in 2019. The acronyms stand for the WHO's classification of regions: AFRO -African Region; AMRO - Region of the Americas; EMRO - Eastern Mediterranean Region; EURO- European Region; SEARO - South-East Asia Region; WPRO - Western Pacific Region. Reprinted from *MI4A Plataform*. Retrieved on March 20th, 2021, p.5, from https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1#:~:text=MI4A%20estimates%20global%202019%20market,for%2068%25%20of%20global%20value. Copyright 2021 by WHO. Reprinted with permission.

Moreover, not only is the vaccine supply is limited, but the demand is also a challenge to be managed. It relies mostly on public purchases for its national immunization schedule, and for epidemic/pandemic vaccines the demand clearly depends on whether outbreaks occur (sometimes this uncertainty can be compensated by advanced stockpiling agreements). Additionally, in recent years an increase in vaccine hesitancy has also threatened to suppress demand (WHO, 2017, p.17).

Therefore, because the vaccine industry is risky, expensive and highly regulated, the public institutions such as in the EU could have a significant role on the vaccine cycle, whether by financing the investigations for new vaccines, regulating the several steps from initial conception all the way to vaccine distribution to be faster for patients, as well as safeguarding demand through inclusion into the national vaccination agenda.

Having in mind this complex environment, it would be helpful to illustrate in a few steps the cycle of a vaccine from research and development to the end consumer, further explained in the subchapters.

Figure 4. 3 *Vaccine Production Process*



Note. Vaccine cycle from research to distribution for regular vaccine and Covid-19. Reprinted from "A Guide to Global COVID-19 Vaccine Efforts" in *Council on Foreign Relations*, by Claire Felter, 2021. Retrieved May 1st, 2021, from https://www.cfr.org/backgrounder/guide-global-covid-19-vaccine-efforts. Copyright 2021 by Council on Foreign Relations. Reprinted with permission.

Grouping the items related with the investigations of the antigen, there is the research and the pre-clinical and clinical trials, otherwise known as R&D. With eventual success of the discovery, registration of the vaccine as a product with the regulatory authorities follows (approval). Once granted the country license, the manufacturer starts the production in scale and distributes the vaccine to accomplish what it ultimately was created to do.

4.1 Research and Development

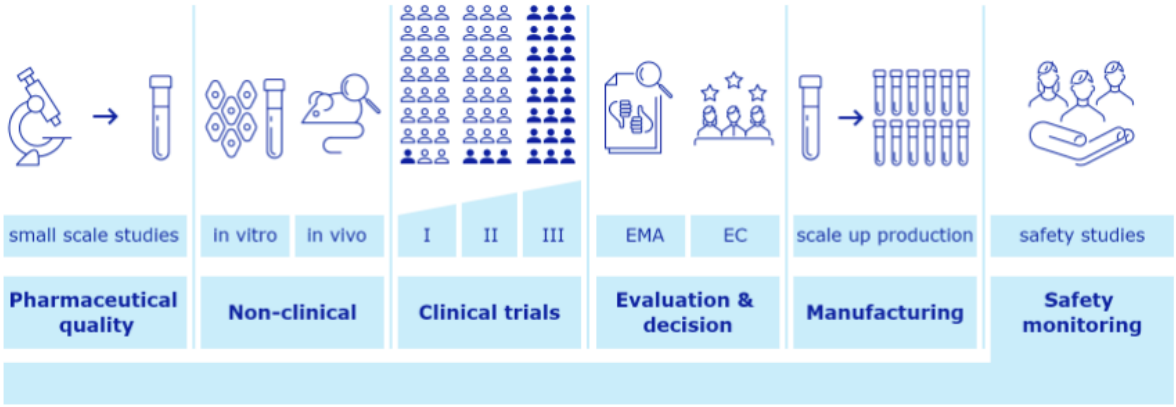
The right R&D strategy at the very beginning of vaccine research can guarantee the appropriate kick-off for a competitive advantage that can reflect in the role of price setting, from manufacturing to end-consumer. This advantage can be translated for instance in developing it quickly to be the pioneer in the market creating a product efficient in a single dose instead of multiple doses, or making the formulation stable in regular freezer temperatures to facilitate the distribution chain.

As mentioned above, the majority of vaccine candidates fail. The success rate from the initial researched idea to the end-point of reaching an approved product is very low, leading to a high risk for public or private investors.

The largest data analysis of probability of success (PoS) of vaccines for infectious diseases done in 2020 using data from approximately 2,500 programs between 2000 and 2020, revealed that the overall PoS for industry-sponsored vaccine development programs is 39.6%. The results are worse when analyzing the non-industry-sponsored vaccine programs: it has a PoS of only 6.8% (Lo *et al*., 2020). These research results are important to inform how risky is the investment in a vaccine candidate and how the sponsor of the biopharmaceutical industry has an important role in bringing new vaccines forward.

Research and development are the longest components in the immunization development. Here, many stages are required to satisfy the standards of safety and efficacy to have a candidate vaccine approved by regulatory authorities, which for Europe is the European Medicines Agency (EMA). Some of these stages can be merged when a pandemic is in place to speed up the cycle but overall there are six stages (exploratory, non-clinical (in vitro and in vivo) and phase I to III) that are worth diving into to provide a complete understanding of the complexity of the vaccine R&D.

Figure 4.1. 1 *Overview of vaccine development and approval stages*



Note. The cycle of vaccine research and development from a regulatory perspective. Reprinted from "COVID-19 vaccines: development, evaluation, approval and monitoring", in *European Medicines Agency*. Retrieved May 1st, 2021, from https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring. Copyright 2005-2021 by EMA. Reprinted with permission.

The many elements of the R&D chain are relevant to be recognized due to its connection with costs and eventually some price determinants. The first stage of a vaccine candidate is exploratory, a small-scale study in which scientists perform laboratory bench research and use tools as computational modeling aiming to identify natural or synthetic antigens.

With a potential antigen found, the second stage is to test it in an animal model (like mice and monkeys). As this phase is not tested in humans, it is frequently called as non-clinical or pre-clinical. The pre-clinical phase involves cell-culture or tissue-culture systems to discover the immune response for a disease. If the outcome is positive in the animals, the study moves further to the following phase, testing the antigen response in humans among three phases with larger numbers of people in each subsequent phase.

In clinical trials, phase I is a small group of about 20 to 100 healthy volunteers, who are checked on their vaccine immune response, safety, and side-effect of doses. If obtained a good response of the antigen and low side effects, the trial progresses to the next phase.

In phase II, the number of subjects is in the hundreds, about 300 volunteers split into different groups by demographics (children, adults and the elderly). The researchers assess the most common short-term side effects, optimal dose, best intervals between doses and the immune response. Once the vaccine candidate has been confirmed safe, it can progress to the further phase with more subjects.

In phase III, the volunteers are the population at risk of the disease that the vaccine studied and aims to protect. This phase requires thousands of volunteers and may last years due to having

to recruit all the required subjects in order to prove efficacy because the incidence of the disease influences the sample size of the subjects. For example: if the disease has a low incidence, it will be required a greater number of volunteers (sample size) to determine the vaccine efficacy. It is a critical stage to secure whether the vaccine is effective, which is defined as the percentage by which the rate of disease incidence is reduced in vaccinated groups as compared to a placebo (Singh, 2016, p 62).

At the end of these three phases, the vaccine developer submits its conclusions to the medicine regulatory authority – EMA and European Commission (EC) to obtain the marketing authorization. The EMA scientifically evaluates the tests results proving whether the new vaccine's benefits are overall greater than its risks and if it attends the quality standards (based on how the vaccine is manufactured, its purity and the ingredients, whether inactive or excipient). The authorities can raise questions and all answers must ensure compliance with EMA's safety standards.

The EC reviews the EMA's expert opinion and authorizes an EU-wide marketing authorization if the outcome is positive. This regulatory approval process can last 1-2 years (an exceptional case for the pandemic is when it can be granted an emergency approval). In Europe, specifically according to the pharmaceutical legislation, the standard timeline for the evaluation of a medicine is a maximum of 210 active days (EMA, 2020, para 27).

Additionally, it is not unusual that regulatory authorities require a post marketing commitment or a post market surveillance study as a condition of the initial authorization given for better understanding of general effectiveness within the population and recording adverse effects which may be experienced after the vaccine is widely adopted.

Finally, having the public market authorization in Europe by EMA, the vaccine developer can start to manufacture in large scale and commercialize the newly approved product. Nevertheless, the authorization by EMA does not necessarily mean immediate access for the citizen to this new vaccine because it still needs to fulfil the requirements for inclusion in the Member-State's health care programs. This inclusion in a country's immunization agenda is sensitive to price, as some new vaccines are reported by governments as too costly to be included in the national schedule (AMF, 2017, p.47). In the EU, a key tool to support Member-States for reimbursement decisions of in-patent pharmaceuticals is the HTA, which assesses the additional clinical benefits of new vaccines against existing ones. However, as each country has distinct ways of interpreting the result of HTA, it may ensue in different prices or different coverage decisions for the same immunizing product across the EU Member States (EP,2011, p.13-14).

The average time lapse between the approval of the EMA for commercialization and vaccine administration to a European citizen is 6.4 years, according to a study of 2013 (Blank *et al*, 2013). Such long-time response from the regulatory perspective, whether from EMA or from a Member-State, has an impact on health accessibility.

Correspondingly in the USA, the economist Milton Friedman concluded that "by now, considerable evidence has accumulated that indicates that FDA [U.S. Food and Drug Administration] regulation is counterproductive, that it has done more harm by retarding progress in the production and distribution of valuable drugs than it has done good by preventing the distribution of harmful or ineffective drugs." (Friedman and Friedman, 1990, p. 205 and 206). This parallel with the American regulatory authority helps to comprehend why the excessive regulation delaying the availability of health commodities is target of criticism.

This lengthy horizon of the vaccine cycle (between non-clinical trials until inclusion of a vaccine in the national immunization programs) together with a substantial risk of failure of the vaccine efficacy/safety are considered as barriers on investment from an industry perspective. According to Pindyck, who was quoted in an article in 2020: "private companies are inclined to delay investment in R&D projects with uncertain returns until the expected profits from the project exceed its cost plus the value giving up the option to delay." (Bloom et at, 2020, p.56). One example given by I. Maitland (2002) fitting this situation is about the Malaria vaccine:

> Even if a vaccine were scientifically within reach, drug makers would hold back (or are holding back). For one thing, since malaria is a disease of the Third World, there may be no market for the vaccine. But as Jerry Sanchs notes, "even if [companies] spend the hundreds of millions, or perhaps billions, to do the R&D and come up with an effective vaccine, they believe, with reason, that their product would just be grabbed by international agencies or private copycats." (pp.460-461).

Not all investment in a vaccine should be under private initiative. As Relman and Angell note, government research agencies and academic institutions are responsible for much investment in basic scientific research (quoted by Stevens, 2007, p.226). It follows that the regulatory authorities, governments and philanthropic institutions can support the acceleration on R&D by promoting guarantees that would de-risk investment in successive stages of a vaccine chain, and by stepping in and guaranteeing a market for vaccines once private companies have developed them. It is particular from the health segment because vaccines are notably a time sensitive commodity, especially felt in epidemics when emerging pathogens are quickly spreading and the access by society should be prioritized to be as fast as possible.

4.2 Manufacturing and Distribution

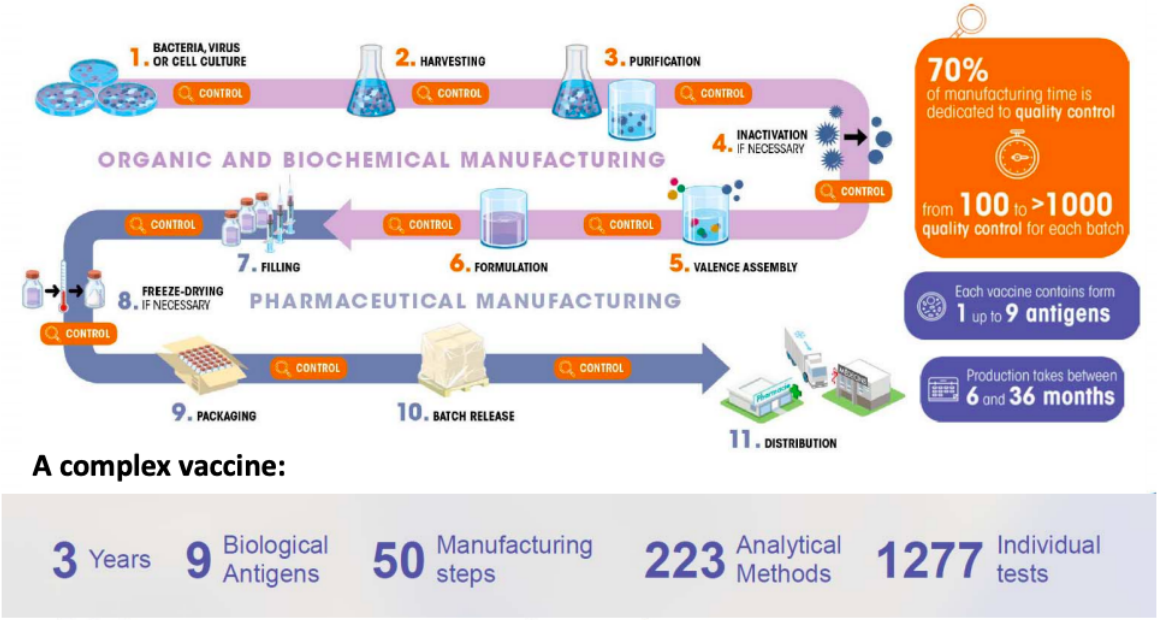
After the detailed steps of R&D supra-mentioned illustrate how an investigation into vaccines is bureaucratic and regulated. It is not a surprise, therefore, that the biological manufacturing process is as extremely regulated and controlled. Besides the vaccine as a product needing to be registered, the manufacturing procedure as well requires formal submission. Every minor modification of the submitted methodology requires another submission to the health authority of Europe.

The manufacturing process takes time, taking overall between 6 to 36 months from agent culture to a batch distribution (Sanofi, 2017) (not considering mRNA vaccine). It is challenging to work with biological components, as storage is time-limited and costly, requiring sensitivity to forecast the production and scale it under pressure of a potential disease breakout, on top of large risks when a batch failure occurs. Running up against a fixed quantity demanded, these production-side factors lead to short-term shortages and price spikes (Mcguire, 2003, p. 208). It is fundamental to align vaccine supply with global demand to avoid disruption through coordination with multiple stakeholders.

All the complexity and level of expertise involved in its production is an industry entry barrier, one of the reasons that vaccine manufacturing is concentrated in just a few large companies, especially concentrated in developed countries. Europe has a strategic role in the vaccine manufacturing because it is responsible for 76% of world supply, distributed across 11 European countries in 27 sites (Vaccines Europe, 2021).

In order to support the understanding of the full cycle of production, the figure below is appropriate. Note that it is illustrating the most common procedure and not covering the specificities of the recent mRNA vaccine technology.

Figure 4.2. 1 *The manufacturing process of a vaccine*



Note. Understanding the complexity of vaccine manufacturing. Reprinted from *Sanofi*. Retrieved February 8th,2021, from https://www.sanofi.com/en/media-room/articles/2017/understanding-the-complexity-of-vaccine-manufacturing. Copyright 2004-2021 by Sanofi. Reprinted with permission.

The full process of production requires a controlled environment, or in other words full control of the humidity, air, temperature and people's access of the space. It accordingly varies the

vaccine type and the part of the manufacturing. For example, the formulation zone requires high purity of air.

Without going into technical scientific details, the chain starts with the development of the antigen (where the vaccine agent can be a virus or bacteria or cell-culture) cultivated and multiplicated to be some sort of cell bank storage. When this stage is ready, it is time to harvest the desired antigen from the microorganism. It is followed by a series of complex chemical and physical procedures for purification and filtrations to isolate the desired agent and maintain it under sterilized conditions which is costly to keep running (Pöri, 2018. P.19-20).

Further moving along in the production chain, the downstream process begins. Some vaccines require a step to inactive the agent (pathogenicity suppression) before inclusion in the formulation. With the active antigenic substances is time to combine to become a single component, to be added with the other ingredients (such as adjuvants, preservatives, stabilizers) during the formulation process.

When finally ready, the vaccine is bottled in a glass vial or already into a syringe, not necessarily packaged immediately. In order to assure the stability and better conservation properties, it may pass through a step called freeze-drying, which removes water by transforming it into power.

The last steps before distribution are packing and batch release. Labelling also follows the regulatory requirements and must have the quality control that assures the safety and quality of the batches before final release to be delivered across the world. Sanofi, a vaccine producer, estimates that 70% of the entire time of vaccine manufacturing is dedicated to quality control through several individual tests (Safoni, 2017).

Nevertheless, the latest step in distribution is also complex, as it requires special packaging or labelling, as well as cold chain transportation and storage (usually temperatures between 2 and 6 Celsius degrees constantly). If a vaccine is stored incorrectly due to a too hot or too cold environment, it becomes improper, rendering the immunizing agent ineffective or inactive. The vaccines are shipped using specialized equipment that does not compromise the integrity of the product.

In long distance delivery, distribution must ensure availability of refrigerated lorries to transport the vaccines from the airport to the warehouse cold room. In regional distribution, portable iceboxes can be used to transport the vaccines until stored in medical refrigerators. In the case of the vaccination taking place in another facility, this will most likely also demand portable ice boxes to transport the goods to local areas, requiring the foresight to provide electricity or special portable devices to maintain the cold temperature for several hours and/ or days.

The manufacturers usually try to develop vaccines taking into consideration eventual local barriers by adapting the vaccine presentation to simplify distribution and administration. Some

features included are, for example: unique-dose presentation, no requirement of cold chain with thermostability, administration via oral or intranasal; all of these reduce the burden on the local supply chain and simplify use by health workers, although developing such features can involve significant cost and require additional regulatory approvals (AMF,2017, p. 64).

As soon as the vaccines are administered to the end user, the national authorities and sometimes also international organizations monitor for possible adverse side effects and responses. Requests from regulatory authorities to run additional clinical trial phase IV (post-approval clinical trial) to regularly assess safety and effectiveness can also be expected.

4.3 Pricing elements

In the previous chapters, which were necessary to understand the complex and unique landscape in which vaccines are introduced, it was illustrated how the research, development and manufacture of an immunizing agent has been lengthy, highly regulated, risky and expensive. Broadly speaking, this process requires a sustained mobilization of highly skilled human and financial resources over a long period of time before any promising candidate reaches its patients (Daems, 2008, p. 5). These notions are important due to the fact that frequently they trigger higher prices, consequently impacting its accessibility to society and full exercise of the right to health.

Chapter 2 of this thesis covered the ethical elements with regard to pricing and its fairness originated from law, morality and solidarity. In the present chapter the focus will be on the economic elements of pricing from firm's perspective when determining its pricing strategy, from government's point of view when assessing value to take decisions and from correlated variants impacting the vaccine pricing in Europe.

One concept of pricing (market price) adopted by neoclassical theory refers to the act of gathering information, conducting quantitative analysis and revealing an accurate understanding of the range of prices likely to yield positive results (Smith, 2012, p. 8). In a perfect market condition, prices indicate the consumer's willingness to pay and thus stimulate manufacturers to produce more of what people want. But the prices also reflect, to a certain extent, the production costs and health markets are notoriously distorted by the presence of insurance and patents, layers of heavy regulation, insufficient information among consumers, and the need to ensure access to effective products, regardless of people's ability to pay (Neumann *et al*, 2021, p. 53).

The challenge for determining vaccine prices pass by multidimensional aspects, impacting the return to the investors but as well as the right to health, as pricing can have a considerable impact on vaccine adoption by a country. Innovative vaccines (usually offering more effective disease prevention) might contribute to increase the pressure in immunization budgets because of their high price while governments have to deal with all other health priorities. According to

the WHO, affordable prices of quality-assured vaccines is one key element to achieve the introduction of new immunizing products in Europe (WHO/UNICEF, 2015, p.2).

Although, according to the Access to Medicine Foundation (2017), not only innovative vaccines have been highly priced, but also some traditional vaccines have become more expensive. This is mainly caused by supply problems (including shortages caused by demand-or-supply-side fluctuations) or due to reduction in competition because suppliers exit definitely or temporarily (in the scenario where very low initial prices were established, which contributed to under-investment in infrastructure, resulting in technical difficulties) (p. 47).

On the other side, the WHO informed that the increasing of mid-size manufacturers and the respective expansion of its vaccine portfolio, mainly in Asia, are often offering more affordable choices due to competition with regional and new vaccine markets, especially for HPV and PCV vaccines (WHO, 2020, p. 4).

It is fundamental to have more clarity in the aspects that drive a firm to set up the vaccine prices in order to avoid the use of their market power to obtain unfair advantages on an important global health solution.

4.3.1 Pricing strategy components

In order to unfold this challenge, Bruce Lee and Sarah McGlone (2010) delved into eleven elements on vaccine pricing strategy from firms which will be used to support this thesis, described below.

1. Target population assessment

Targeting the population is important, especially segmenting them because, depending on the immunization agent, it can have different efficacy and therapeutic indications endorsed by influential health committees. Hence, firms normally compile an extensive market analysis, identifying and characterizing potential populations, purchasers and utilizers.

For instance, the prices for a pediatric vaccine might take into account if the bills are covered by parents and/or their insurance, differently from a product targeting older adults which the funding is likely to be covered by medical insurance.

2. Potential competitors and alternatives

The final price of a new vaccine is influenced by competition, even a potential competitor or own manufacture previous generation products. Starting with lower prices may promote higher acceptability by countries, influencing its adoption into their national immunization agenda as well as prompting competitors to lower their prices.

Setting up a higher price than a competitor can be justified when the new vaccine offers distinguished technological advantages that translate into a recognizable clinical difference to

the patient. Seemingly a risky strategy, it eventually can lead to increased investment in the vaccine industry if it becomes a "blockbuster", as in the examples of Prevnar (for pneumonia) and Gardasil (for HPV).

3. Target product profile (TPP)

The TPP is used to plan research and development processes through listing of the features that a new vaccine would have when it reaches the market in 3 scenarios: optimistic, realistic and pessimistic. It determines pricing as it plans key elements like target disease, way of administration, comparative efficacy, improved convenience for the patient/health worker, possible side effects and compare all that variants with current available vaccines (from the own manufacturer or competitors), supporting the price decision-making.

4. Incremental higher value

If identified that a new vaccine has distinguished characteristics, the vendor will quantify this technologically added value into incremental higher prices. In simple terms, how much more they can charge with more efficacious, safe, or convenient administration.

5. Marketplace position

A vaccine is introduced in a due market depending on the manufacturer's needs and interests in regard to the available market and the strengths/weaknesses of the product's dynamics. Frequently it is assessed if the new immunizing agent will be a lower cost alternative or a superior product, or a complement to existing products in order to position it on the market. The example given by the academics above mentioned was that Gardasil positioned targeting a disease; an anti-cancer vaccine versus Recombivax HB positioned as an antiviral vaccine.

6. Price-demand curve

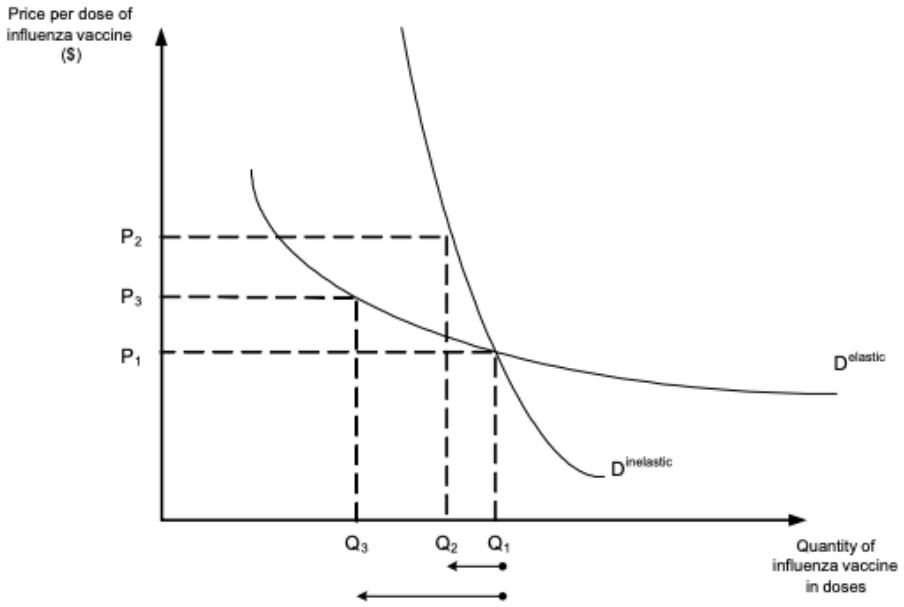
In determining price, it is key to understand the price elasticity of demand, or in other words, how the vaccine price would affect the purchase by public or private stakeholders. Accordingly, the more the demand is impacted by price, the more elastic the demand becomes.

The vaccine price-demand curve mostly depends on the urgency of the threat and competitor options, but as the vaccine market is concentrated in a few suppliers, this element might not play a critical role when compared to other health therapies (except for off-patent vaccines in which competition is possible, as they are not protected by intellectual property). A product for imminent threats like rabies and tetanus will be more likely to be inelastic as demand would not be affected by a variance on prices. Oppositely, if demand is highly elastic, then even small price increases could lead to significant reductions in the quantity of doses sold (example on figure 8).

Helping to put this into perspective is a study by researchers in 2005, where they analyzed the elasticity of influenza vaccines in 2000-2001 during the influenza season in the USA. Heinrich found that when vaccine shortfalls arose because of manufacturing delays, one buyer reported paying $12.80 per dose for influenza vaccine, when they previously paid $2.87 per dose just

some months before the influenza season. Therefore, the pricing does not appear to limit influenza vaccine output significantly, demonstrating inelasticity (Nevel *et al*, 2005, p. 11-13) as below graphically informed in figure 4.3.1.1.

Figure 4.3.1. 1 *Price Elasticity of Demand for the Influenza Vaccine in 2000-2001*



With elastic demand, a small increase in price (P_1 to P_3) will cause a large reduction in quantity demanded (Q_1 to Q_3). With inelastic demand, a large increase in price ($P_1$to P_2) will cause only a small decrease in quantity demanded (Q_1 to Q_2).

Note. Influenza vaccine price elasticity's curve in 2000-2001. P represents price, D demand and Q quantity of vaccines. It aims to evidence inelasticity as the pricing change (P1 to P2) does not appear to limit influenza vaccine output significantly (Q1 to Q2). Adapted from "Influenza Vaccine Economics", by A. Nevel, A. Honeycutt, T. Robinson, C. Layton, 2005, p.12.

7. Vaccine costs

The cost of a vaccine includes its R&D, manufacturing and distribution, although it can also comprise sunk costs of unsuccessful R&D initiatives, cost of opportunity and mergers, acquisitions and exchanges of intellectual property that might occur in the industry.

The manufacturing costs depend on the immunization type, technologies used, possible obstacles, and the concomitant development and production of other products, additionally on the high fixed costs of establishing and maintaining a vaccine manufacturing plant, specialized personnel and facility depreciation. Hence, unless a manufacturer already has facilities already in operation and is selling a very high volume of vaccines, lowering vaccine prices may be difficult.

8. Costs for legal, regulatory, third party payer and competitor factors

Biopharmaceutical manufacturers rarely have full prerogative to set up a new vaccine price, as the range is limited by governments, legal authorities, regulatory agencies and competitors. Legal constraints prevent prices from being too high (price gouging) or too low (predatory pricing / dumping), largely varied for different populations (price discrimination), or too similar to competitors (collusion). Usually, the prices of existing competing or alternative products can be used as a precedent for new vaccine pricing.

9. Overall product portfolio

When the manufacturers have a robust portfolio of health products, they also have more flexibility on pricing because they can use their full portfolio in their pricing strategy, potentially to increase or decrease profit margins, which may include other options than vaccines (such as medicines and medical equipment).

10. Pricing objectives

Under capitalism logic, maximizing the profit is the common objective of manufacturers, and what will differentiate is the path chosen to achieve those gains. Manufacturers' most common pricing objectives mainly enumerated by Bruce Lee and Sarah McGlone are:

- *Maximize adoption of new vaccine:* frequent when targeting large populations - if achieved, economies of scale producing will be less expensive per vaccine.
- *Maximize profit-margin:* often when potential sales volume is low, as when targeting small/specific populations.
- *Maximize revenues:* option when is it expected that vaccine costs will not keep proportional to initial profit baseline (e.g., when costs decrease in subsequent years after the recovery of an initial investment in production). This strategy can be used for long-term, if firms are able to have larger market share, even if it means a reduction in short-term profit, it can trigger market concentration and so increasing profits in the long term by having more consumption.
- *Recover costs:* simply recoup some or all of the costs of developing and manufacturing the vaccine.
- *Signal quality:* higher prices be perceived as higher quality to consumers, even if this model is less pervasive in the vaccine industry; prices well-below similar vaccines may raise quality concerns among purchasers, especially for a less well-known producers.
- *Facilitate product survival:* benefit in a market by having a certain vaccine (even if non-profitable) to maintain relationships with purchasers or ease introduction of other more profitable products.
- *Benefit associated products:* the vaccine price may facilitate the rest of a manufacturer's product portfolio, especially when products are sold together.
- *Maintain status quo:* price is setup to keep similar market share.

11. Pricing structure

A vaccine price will be setup normally between the lowest cost-driven price (cost of production and distribution) and highest demand-driven limit (above there is no will of purchase). Some pricing strategies are more focused on vaccine costs, like the cost-plus pricing (price is vaccine cost plus a profit margin) and target return pricing (price level set to achieve a specific return-on-investment). While other core strategies are on vaccine demand like demand-based pricing. Moreover, a major part of vaccine pricing structure considers discounts, promotions and other types of incentives that lowers the effective price paid by the buyer, frequently linked with the volume purchased or specific to certain geographic regions, populations, and times of the year. According to a McKinsey report of 2006, firms can create a consistent database to guide its pricing decisions and measure their impact if methodically capturing information in a pricing support tool, though this potential source for strategic decision is not used in its full capacity, quoting:

> Unfortunately, despite the increased sophistication of pricing software, companies still have great difficulty extracting the insights they need to improve their performance in this area. The information required to develop these insights – product volumes, list prices, promotional spending, trade allowances, payment terms, and data on the cost of products, for example – typically resides in a broad array of isolated systems run by finance, sales, logistics, and customer service (McKinsey, 2006, p. 75).

Robert Pearl, comments that the high prices performed by the health companies, regardless of the elements or criteria currently guiding the firm's decisions, are based on profits, not on moral, ethical or societal considerations (Pearl, 2019, para 11).

4.3.2 Value-based pricing

The Member-states in Europe based their decision to introduce a new vaccine not oriented solely by lower prices. Despite affordability being a key element, they usually make an evidence-informed decision following the advice of the National Immunization Technical Advisory Group (NITAG) using WHO guidelines, as follows:

> (1) The disease, including its burden, public health or political priority, and the availability of other prevention and control measures; (2) the vaccine, including its efficacy and safety, economic and financial issues and supply availability; and (3) the strength of the immunization programme and health system to accommodate the vaccine. (WHO, 2018, p. 44)

Often to support the decision by a country to adopt a vaccine on its immunization schedule or to evaluate the levels of reimbursement, a value-based analysis by the perspective of a health system and society is required to incorporate the added value of social benefits to inform pricing. Obviously, it does not mean that the vaccine producers should capture the entire social

benefit of a vaccine by increasing its price. The value-based methodology is a target of criticism from different non-economists due to the notions of justice omitted in the valuation.

In particular, there are two well-established value-based economics tools to evaluate health interventions by governments: Cost-effectiveness analysis (CEA) and Cost-benefit analysis (CBA). The goal of CEA is to compare the relative costs and relative effects of two or more courses of action, for example: how much does it cost to save a certain number of lives, years of life gained from the intervention or to avert a certain number of illnesses and surgical procedures. The second method, CBA, aims to directly compare cost and benefits by monetizing the value of the latter. Both methodologies receive criticism because neither takes into account the cost of averted later infections to measure the future cost savings (as it is difficult to predict) and the lack of inclusion on the impact of health in incomes (Stevens, p. 215-216).

Some authors suggest measuring value through cost-utility analysis (CUA), a type of cost-effectiveness analysis which uses quality-adjusted life years (QALYs)- a ratio of each incremental cost of intervention to its incremental benefits. So, lowering the ratio is more recommended as the vaccine would produce health gains at the lower cost. The use of cost-per-QALY ratio has been considered as the "gold standard" for value-based calculations because it represents the number of years lived added by the intervention, considering also the patient's quality of life. Additionally, other metrics could be used such as avoided deaths, life-years saved, disability-adjusted life years (DALYs). But it is limited as well and could potentially contribute to unfairness when omitting health access to people with conditions that are more expensive and not take into consideration fear of contagious diseases and impact in the low-income population (Neumann, 2021, p. 55-56).

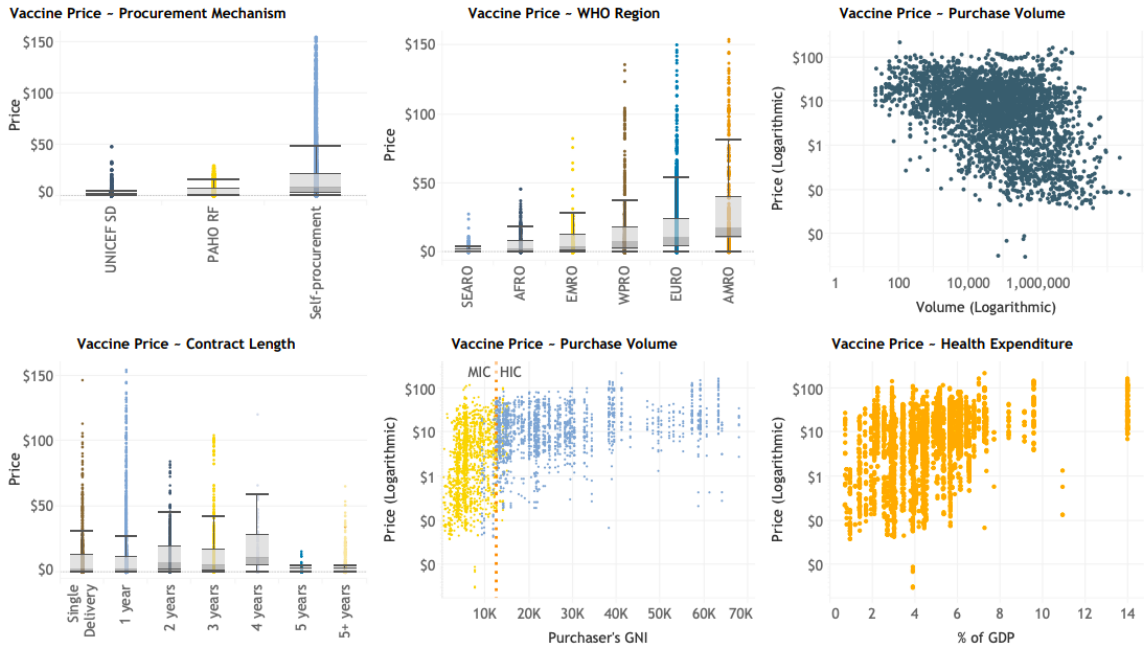
On the discussion regarding the value-based pricing, the question of whether the government contributions to R&D should take into consideration or not stands out, as it is difficult to measure directly the public contribution to the market vaccine, as virtually all industries benefit from R&D. According to Neumann *et al* (2021), the governments invest in research because it is a public good and because if it is left to private initiative it won't persecute the main needs of the society, and the health industry pays back for public investment profited by them through taxes rather than lowering prices (p.58).

Whether the metric of the benefits is reported, vaccination is universally considered as an important public health instrument with effects that translate into positive economic outcomes. Given the above, a pricing analysis that take into account the full value of a vaccine to society and health systems can guide regulatory agents to consider a full landscape of costs and benefits associated to take a decision and improve future population's health given resource constraints. But they must not revert the value captured in increasing vaccines prices to biopharmaceutical producers.

4.3.3 Correlations of factors impacting price

Despite the common elements determining price such as number of competitors and number of alternative solutions, the vaccine market has its particularities and limitations that make the price less elastic compared to other commodities (Mcguire, 2003, p.209).
Therefore, we shall consider 3 main elements impacting the variation of vaccines' prices reported by the WHO that will be reproduced in this subchapter (WHO, 2020, pp. 6-8): procurement mechanisms used, contract length, and volume purchased.

Figure 4.3.3 1 *Correlation factors impacting vaccine price*



Note. Correlation of vaccine price by factor worldwide. Reprinted from *MI4A Plataform*. Retrieved on March 20th, 2021, p.6, from https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1#:~:text=MI4A%20estimates%20global%202019%20market,for%2068%25%20of%20global%20value. Copyright 2021 by WHO. Reprinted with permission.

Delving into the correlations illustrated above, the price seems to be closely connected to the manner of purchase, although there are different prices across vaccines and income groups. UNICEF SD (Supply Division) and PAHO RF (Revolving Fund, for countries and territories of the Americas) have pooled procurement mechanisms for multiple countries while self-procurement represents an individual country purchase. Accordingly, using pool procurement, 21 of 28 vaccines had lower prices versus self-procurement, and on average 60% lower vaccine prices for MIC procuring from UNICEF or PAHO versus non-Gavi MICs.

The advantage of pooled procurement mechanisms is that it enables larger volumes than individualized orders, so because of greater volumes they can leverage into the negotiations to obtain lower price per dose, minimizing uncertainty on demand for the manufacturers.

Conversely, self-procurement purchases showed less clear impact for the same variables (order volume and contract length) under a multiple linear regression (MLR) analysis. According to the report: only very large volume purchases result in a reduced price – a decrease of 1.8% of vaccine price per additional 1 million doses purchased. The length of contract on price was statistically insignificant, except for specific vaccines (which was enough data to run independently): PCV, HPV, HepB, BCG, and MMR.

Furthermore, the WHO assessed the impact of income level and willingness to invest in health spending (measured by health expenditure as a percent of GDP) on self-procured vaccine prices, which showed to not be clearly linked to income. Despite self-procuring HICs pay five times more than self-procuring MICs in a simple average pricing assessment, at the country level, prices paid by MICs and HICs substantially overlap.

In line with the rationale that a higher willingness to pay results in lower price sensitivity, higher health expenditure as a percent of GDP is associated with higher prices in the WHO analysis.

It is relevant to strengthen the database of vaccines to better understand the dynamics of demand, supply, pricing, and affordability to assist further decision-making and policies. In Europe, the predominant way of procurement is self-procurement (67%), and a pooling process represents only one quarter of vaccines purchased (24%) (WHO, 2017b, p.3), most likely because of the health framework that based in national prerogatives rather than as a collective block.

Therefore, there is significant space to achieve lower prices by shifting the individual national procurement to a centralized European pool-procurement. The use pooled mechanisms would as well allow greater flexibility, and to create more equitable access given limited production capacities at the global level (EU, 2013). Only in 2014 a pooled instrument was introduced in the EU - the European Joint Procurement Agreement (JPA) - in the context of preparation for pandemics after the H1N1 pandemic of 2009. Still early to translate the economic benefits of JPA on the Covid-19 pandemic, however, there are already suggestions that this pooled tool is underpinned by a growing level of political willingness and mutual trust (Mcevoy *et al*, 2020, p.15).

4.4 Why are the price of vaccines high?

Finally, a pertinent question makes itself present: why one of the most cost-efficient lifesaving solutions has high prices? Sounds like an irony: an item with high social value, but with weak incentives to be developed.

Laurie Garrett, a global health policy analyst answered this question. According to him, by 2008 the prices of vaccines became so cheap (about 0,60 cents of dollar for each vaccine) that they did not provide the market incentive to keep companies in activity. Despite the high demand in volume for vaccines, the low profit margins have long blocked the vaccine pipeline, and consequently only a few companies were interested in staying in the vaccine business (Garrett, 2017, para 8). As previously detailed, the vaccine cycle is extremely complex, as it is long (8-15 years), bureaucratic (tight regulated), risky (uncertainty of successful candidate and future demand), and expensive (R&D and manufacturing costs); if all these barriers are not compensated by higher return (higher profit) the private companies will lack motivation to stay in the market. Thus, all these factors make a higher return necessary to attract investors (or firm developing vaccines programs) which explain high prices.

It would be illustrative to have a comprehensive view of the prices for a certain vaccine and region on a long horizon of time to assess its variance and determine if low or high relatively to GDP or peers, but the low availability of databases for historical prices renders a robust analysis on price evolution impossible. In order to fill the gap, the WHO and UNICEF under the V3P and MI4A initiatives are shedding light on this relevant information and gradually enlarging a public database. The latest data released on vaccine prices variance in European countries are dated from 2016 (figure 4.4.1) and it is interesting to be shared to give a glance of how the pricing elements mention can lead to different outcomes.

Figure 4.4. 1 *Minimum, median, and maximum of vaccine prices in Europe in 2016*

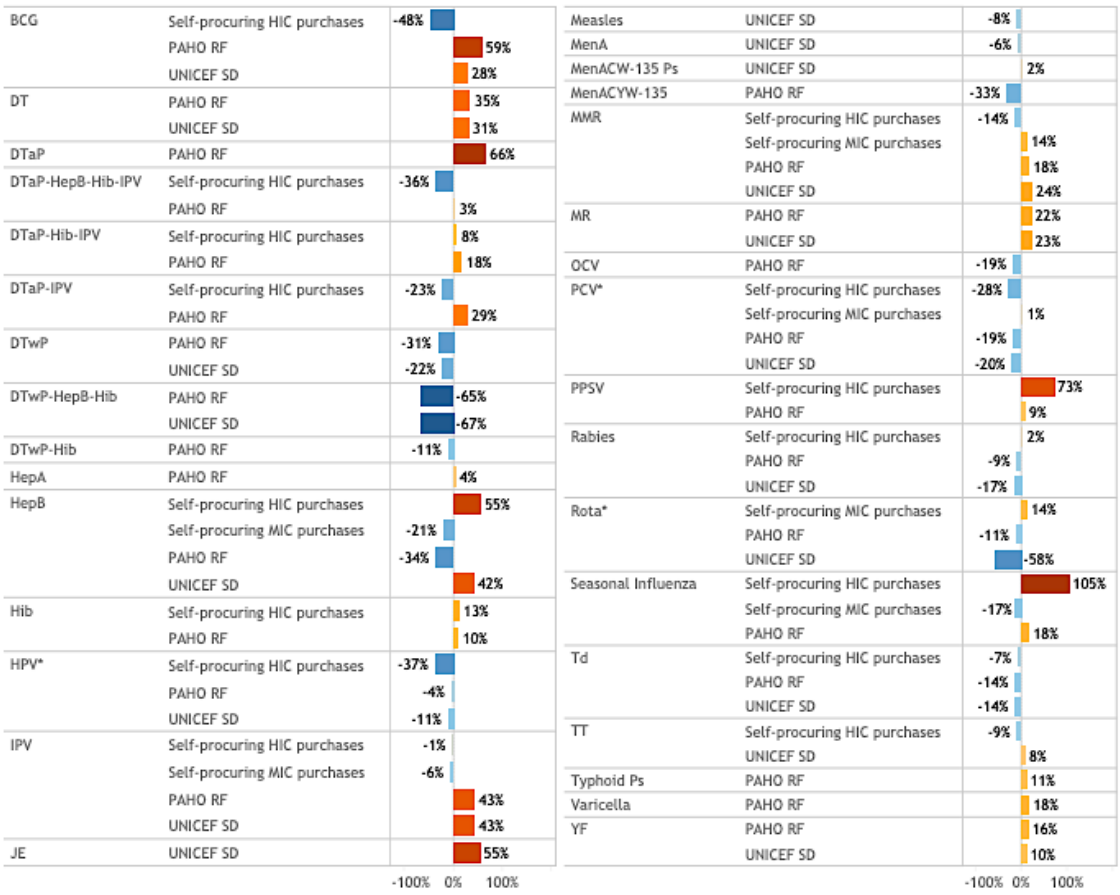
Vaccine type (ranked by frequency of use)	% of countries self-procuring in EUR	EUR price (all procurement methods, all income groups): lowest (presentation size) / highest (presentation size) / median	N different products in EUR	N manufacturers in EUR	N manufacturers reported globally
MMR	69	$1.10 (5-dose) / $15.78 (1-dose) / $5.66	8	4	5
BCG	50	$0.06 (10-, 20-dose) / $2.77 (20-dose) / $0.46	11	8	16
HepB (ped)	54	$0.06 (10-dose) / $15.00 (10-dose) / $0.85	9	6	13
PCV	68	$3.14 (1-dose) / $77.59 (1-dose) / $31.24	5	2	2
Td	50	$0.06 (2-dose) / $10.07 (1-dose) / $0.18	11	8	13
DTaP-Hib-IPV	82	$13.76 (1-dose) / $41.89 (1-dose) / $22.19	4	3	3
DT	38	$0.11 (10-dose) / $7.24 (1-dose) / $0.15	8	6	11
DTaP-HepB-Hib-IPV	87	$17.70 (1-dose) / $78.85 (1-dose) / $39.71	3	2	2
Influenza (seasonal – adult)	79	$1.01 (1-dose) / $7.92 (1-dose) / $4.65	7	6	11
bOPV1,3	23	$0.14 (20-dose) / $1.86 (20-dose) / $0.18	4	3	10
HPV	92	$15.00 (1-dose) / $154.13 (1-dose) / $47.05	3	2	4
DTaP-IPV	92	$8.18 (1-dose) / $26.63 (1-dose) / $15.19	2	2	2
DTP	17	$0.13 (2-dose) / $3.01 (10-dose) / $0.21	5	4	8
HepB (adult)	75	$0.59 (1-dose) / $55.45 (1-dose) / $4.99	7	5	10
IPV	82	$1.97 (5-dose) / $13.42 (1-dose) / $4.71	5	3	7
Rabies	73	$5.69 (1-dose) / $50.25 (1-dose) / $13.31	6	6	7
TT	89	$0.06 (2-dose) / $6.77 (1-dose) / $2.09	6	5	14
Rota	22	$2.05 (1-dose) / $76.44 (1-dose) / $5.34	2	2	3
DTP-HepB-Hib	0	$1.57 (10-dose) / $2.82 (1-dose) / $2.35	4	3	11
Hib	88	$3.66 (1-dose) / $17.94 (1-dose) / $6.43	4	3	4
Varicella	86	$17.50 (1-dose) / $141.93 (1-dose) / $44.28	2	2	4
Pneumo ps	100	$11.09 (1-dose) / $59.35 (1-dose) / $16.92	2	2	2
DTaP	86	$9.52 (1-dose) / $27.92 (1-dose) / $15.46	3	2	3
HepA (adult)	100	$13.20 (1-dose) / $35.37 (1-dose) / $19.73	3	3	4
HepA (ped)	83	$7.50 (1-dose) / $24.73 (1-dose) / $17.08	3	3	9
Tdap	100	$8.53 (1-dose) / $16.64 (1-dose) / $14.95	3	2	4
Typhoid	100	$2.58 (1-dose) / $47.26 (1-dose) / $14.64	3	3	3
MenC	100	$16.35 (1-dose) / $37.09 (1-dose) / $23.84	2	2	3

Note. Proportion of countries self-procuring with minimum, median, and maximum prices, number of products, and number of manufacturers for each vaccine type reported in 2016. Reprinted from *MI4A Plataform*. Retrieved on 3rd March, 2021, p. 4, from https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/V3P_Region_Fact_Sheet_EUR.pdf . Copyright 2017 by WHO. Reprinted with permission.

The above figure demonstrates the majority of immunizing products in Europe are self-procured, with significant variance of minimum and maximum prices, especially for PCV and HPV, which potentially could indicate a non-compliance of fair prices or a missing opportunity by countries to bargain lower prices. All have manufacturers present in Europe but the quantity of competitors with Europe could vary largely depending on the kind of product, for example, the MenC vaccine has only 2 producers while BCG has 11.

In retrieving similar public reports (2020) of worldwide vaccine pricing data between 2014 and 2019 to try to track variances on pricing, however, does not show a clear increase or decrease, but individual analysis by country and/or vaccine showed evidence of increased prices in high income countries (HIC) when self-procuring and a decrease in prices for 4 products (DtwP, DtwP-HepB-Hib, PCV and Tb) most likely due to donor interventions and increased supply competition (WHO, 2020, p. 7).

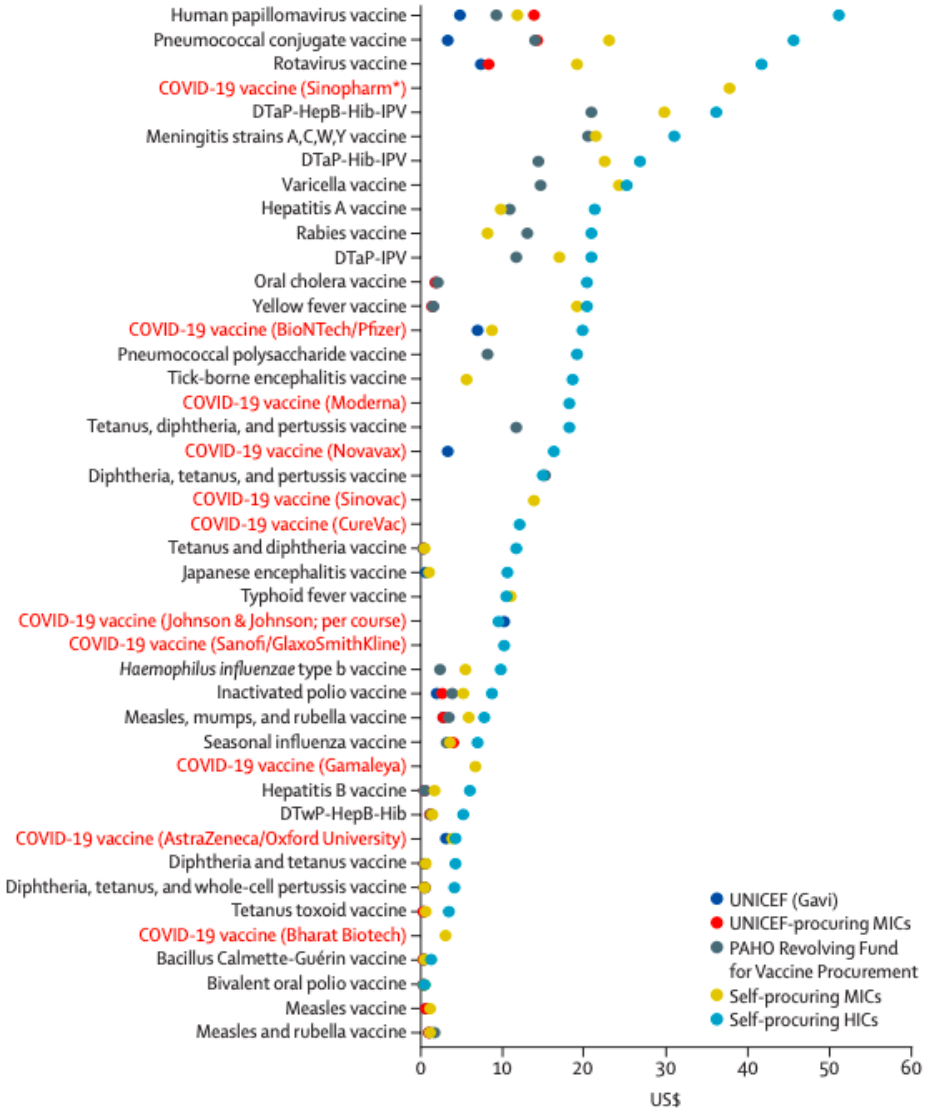
Figure 4.4. 2 *Percent change in average price over time 2014/5–2019*



*UNICEF prices for HPV, PCV, and Rota are the price offered to Gavi-supported countries only.
Note. Average percent change in price from 2014/2015 to 2019 globally. Reprinted from *MI4A Plataform*. Retrieved on March 20th, 2021, from https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1#:~:text=MI4A%20estimates%20global%202019%20market,for%2068%25%20of%20global%20value. Copyright 2021 by WHO. Reprinted with permission.

A similar trend of higher prices for HIC self-procurement for Covid-19 vaccine was found by a recent study conducted by multiple researchers and published in The Lancet in the figure 4.4.3. Such data trend could inform, to a certain extent, that the prices of vaccines are high because European countries are buying by their own (self-procurement) losing an opportunity have lower prices by higher volume purchased (if bought in group) and decreasing the risk of demand oscillations for the manufactures.

Figure 4.4. 3 *Median prices for COVID-19 vaccine and existing vaccines*



Note. Median price per dose for leading COVID-19 vaccine candidates and existing vaccines by procurement or country income group. Data for existing vaccines obtained from the WHO Global Vaccine Market Report as of 2018 and data for COVID-19 vaccines are as of Feb 3, 2021 from press releases, investor documents, and media reports. country. Reprinted from "Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment" by Wouters, J.; Shadlen, K.; Salcher-Konrad, M.; Pollard,A.; Larson, H.; Teerawattananon, Y.; Jit, M, 2021, The Lancet, Volume 397 (issue 10278) ,p.1027. Copyright 2021 by Elsevier Ltd.. Reprinted with permission.

It is worth illustrating the pricing discussion with the most recent vaccine available to defeat the pandemic. The Covid-19 vaccines are especially relevant, as countries are aiming to obtain herd immunization and need to supply nearly their entire populations, so depending on the price that these immunizing products are charged, it potentially becomes unaffordable for many governments. Additionally, there is a potential for the Covid-19 vaccine to be a recurring expense, depending on the duration of protection offered and protection against new variants.

Unfortunately, in the WHO's data collection there was no clear trend in price by the vaccine group, for instance, if whether it was based on traditional technology or innovation. Also, the limitation on the data collection per se, many vaccines have only one procurement group for analysis (either because the sole use in certain markets or due to a limited number of country-reported records available for self-procured purchases), which renders the report not extensively informative. Nonetheless, it is already an important step towards transparency.

From a biopharmaceutical firm perspective, the time horizons to recover the high investment made is accompanied by substantial risk of failure of the clinical trial and risk of unprofitability due to the low ability to pay off in important markets and competition from other vaccine developers, as well potential substitutes (an example being effective antimicrobials and other biomedical countermeasures) who could demand that firms compensate with higher returns to their investors.

The intellectual property (IP) rights (including market exclusivity periods and supplementary protection certificates) also represent a further challenge in this pricing dynamics. Differently from other health treatments, which can be used multiple times or used for a lifetime, the vaccine is frequently administered only once or twice (in the case of a vaccine booster), and consequently the producers need to gain the return on its investment from a single dose. Therefore, it is expected that the manufacturer will be particularly interested in protecting the vaccine patent to ensure a time-limited monopoly, pricing high markups above production costs without further government barriers for at least 20 years over the patent time (Stevens, 2007, p.225-226 and Mcguire, 2003, p.209). Accordingly, a low competition environment lacks the market force to push prices down, complementing the factor of high prices.

Complementing the IP dynamics on pricing, it worth to mention when this corporative right can be relaxed. In a medical state of emergency, invoking the public health interest, the

countries can call for a compulsory license (CL) - situation which allows local companies to manufacture "generic" vaccines for internal use and to export to countries that lack their own production capacity with fair compensation to the patentholder. The CL is allowed by the World Trade Organization (WHO) under the Trade-Related Intellectual Property Rights (TRIPS). The reflection of the CL in pricing could vary, might result in a global decrease of prices of the original patent holder due the threat of losing the monopoly secured under a patent, or a global decrease in pricing caused by multiple competitors in the market.

In 2021 with the pandemic of Covid-19 devastating the world's population for more than one year, the compulsory license gained presence in the media with calls to drug companies withdraw its patents. One loud call was an open letter signed by 150 public leaders to support the IP waiver and addressed to the American president. Illustrating with some of the arguments used by advocates of IP relaxation, Dr. Jeffrey D. Sachs:

> The benefits of mRNA and other IP should be made available globally without further delay, and the knowhow should be shared as rapidly and widely as possible. We have the capabilities to scale worldwide immunization, in order to save lives, prevent the emergence of new variants, and end the pandemic. IP must serve the global good, rather than humanity serving the interests of a few private companies. (Saches, 2021, para 13).

The arguments of keeping the IP on Covid-19 vaccines seem weak when the entire public health is in the stake and the supply cannot accommodate the sudden demand or prices are limiting the accessibility of a life-saving commodity.

4.4.1 Arguments supporting high prices

Because health is a right, every blocking point preventing society to usufruct it becomes polemical. An advocate of free pricing for the pharma industry, Ian Maitland (2002), translated well into words the duality in question:

> "Drug makers are whipsawed between conflicting public expectations. On the one hand, they are expected to maintain the flow of new life-saving and life-enhancing medicines. On the other, they are exhorted to price their products "responsible" and ensure that they are affordable. We rely on the profit motive to mobilize vast resources to fight disease, but we are shocked when new drugs earn excessive" or "obscene" or "windfall" profits. We enjoy the fruits of capitalism, but we expect firms to behave a little less capitalistically." (p. 453).

The literature in favor of high prices on vaccines has mainly two argumentative lines: one based on incentive to innovate and the second on replacing/cost-avoidance of more expensive health solutions.

In the first line of argumentation, some authors (Scherer, 2001 and Grabowski and Vernon, 2000) devolved the idea that the high prices are a compensation for the high and risky investment in R&D, and that this premium price would keep the incentive to drive innovation. The author Ian Maitland (2002), for instance, is also in favor of pricing the health therapies not driven by ethics but from profit, and according to him the profits incurred in the present will become the health solutions of the future: "Price controls notoriously create shortages because they take away incentives to invest in producing more of an existing product/or in developing new products. […] so, price controls on drugs will slow the development of new drugs." (p. 458).

Moreover, the biopharmaceutical industry has long been using the same argument, attributing that the enormous costs of R&D are only sustainable by the prices charged for the subset of drugs that are finally approved (Stevens, 2007, p. 226).

A counter argument for firms asking prices that are not proportional to the real development cost pass by the other public incentives they often receive to support R&D like grants and favorable tax schemes (Schoonackers, 2020, p.18). Recently, this discussion gained more visibility with the context of the Covid-19 pandemic and the impressive values flowing towards vaccine research, development and manufacture of approximately 10 billion dollars given by governments (mostly the US) and non-profit organizations (Wouters, 2021, pp.1025-1026). As so, economists and advocates for accessibility are arguing that ownership and prices of new medicines must reflect these high non-private investments. This could be the explanation behind the lower price of the Covid-19 vaccine offered to high income countries which supported the R&D at earlier stages, such as Pfizer's lower prices per dose in EU ($14.70) in contrast to the USA ($19.50) (Tomlinson, 2021, para 19-20). It is important to mention that such a line of argumentation could as well be reframed and be used as a justification to charge higher prices to low and middle-income countries not able to contribute to R&D.

The above-mentioned second pillar of argumentation in favor of high prices claims that the vaccine, in some cases, substitute more expensive therapies and can even improve quality of life, providing savings to governments (Cutler *et al*, 2021, Rémy *et al*, 2015 and Berndt *et al*, 2002). In order to provide some perspective, the WHO estimated that with the polio eradication, governments would save up to 1.5 billion dollars per year in vaccines, rehabilitation costs and treatments; GAVI estimated that direct savings in health care were 275 million dollars per year with the elimination of smallpox (Stevens, 2007, p. 228).

An example of economic analyses found out that several expensive new vaccines were cost-effective based on common thresholds in Europe such as t20,000 to t50,000/QALY, in other words: these vaccines would provide good health value at a cost deemed reasonable followed by buyers' willingness to pay (Drummond, 2007, pp. 17-21).

A study sponsored by the biopharmaceutical company Sanofi (Quilici *et al*, 2015) suggested that public investments in vaccination can have a significant return on investment caused by

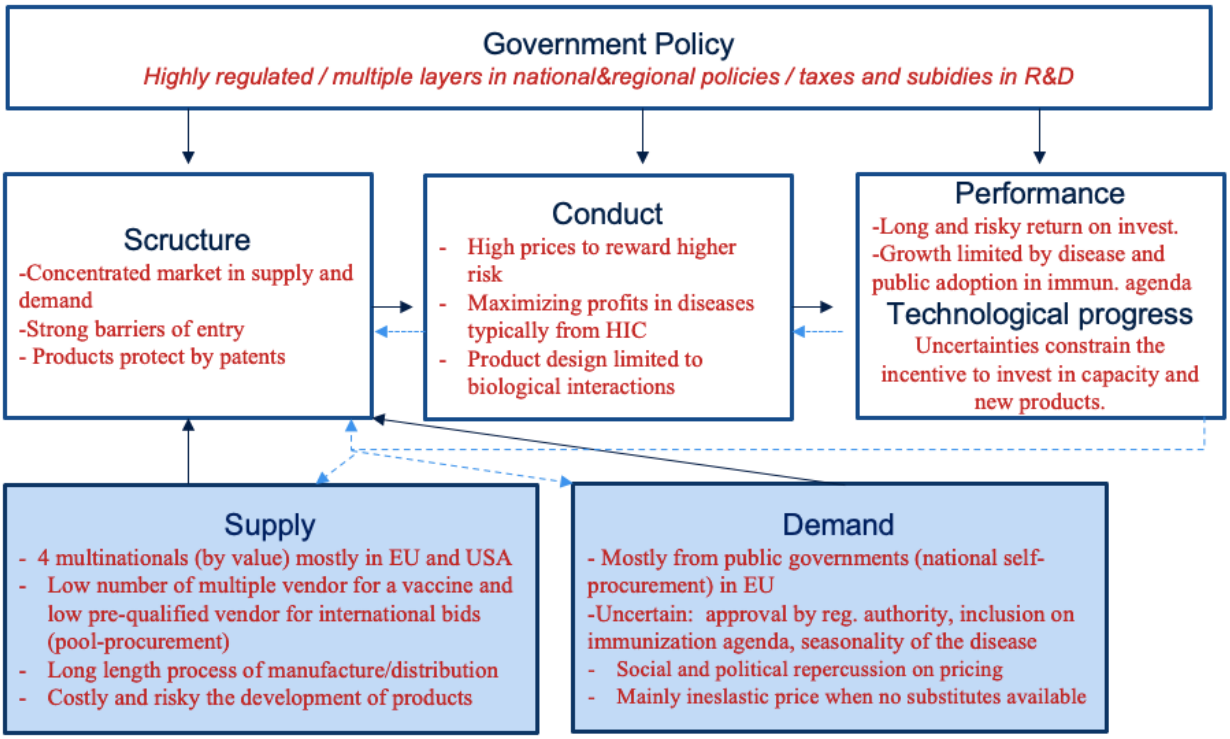
reduced government expenditure and increased tax revenues if considering macroeconomic models with elements such as the life course of average citizens (average schooling, employment, marriage, wages, and pension costs), productivity, reductions in mortality, morbidity contributing to increased consumption, and gross domestic product (pp. 1-7).

The cost-effective justification has not been fully investigated by literature, as studies had been found difficult to generalize due to a great variation depending on how the vaccines were delivered (Pegurri *et al*, 2005) and due to the uncertainty around model assumptions (such as perspective, model design, time horizon and comparators) (Rémy *et al*, 2017, p.4). While cost-effectiveness analyses are useful to inform decision-makers about vaccine adoption, using it to justify high prices by the manufacturer would unduly entitle them to capture social and economic added value disproportionally of fair market prices and affordability.

4.4.2. SCP Paradigm for vaccine

On the whole, it seems that the vaccine pricing is surrounded by factors contributing to keep its prices high as detailed in previous sections in this thesis. Through the support of the SCP paradigm as an analytical framework, a summary of the main variants in the vaccine industry which are reflecting on the high prices patamar was displayed in figure 4.4.2.1.

Figure 4.4.2. 1 *Challenge cycle impacting vaccines pricing by SCP paradigm*



Note. Structed-Conduct-Performance paradigm on vaccines industry in summary. Created by the author.

The EU and Member-States interplay a peculiar role in the vaccine market because health is a fundamental right, and the immunizing agent is an important tool to safeguard this right. Thus, they have simultaneous positions reflecting on the *Structure, Conduct and Performance* of the vaccines in Europe due to their multiple function as a policy maker, regulatory authority, provider of funding, and main purchaser.

The European market for medicines, especially for bio components as vaccines, is extremely regulated both centrally in EU or nationally (at Member-State level) with multiple and heterogenic compliance levels to satisfy the regulatory authorities' level of safety and efficiency since the clinical trials until vaccine's distribution (and even post-marketing). Those complex *Government Policy* is contributing to make the vaccines process bureaucratic, long and costly for the manufacturers, promoting harder barriers for new entries. Thus, it is gathering the conditions to have in the *Structure* just few firms able to meet the standards of quality established by the authorities. Accordingly, it sounds logical the preference of the European countries to purchase from local or regional sellers (recall figure 4.2), likely those vendors are already adapted to the heterogenic norms of each Member-State.

Moreover, a successful vaccine is costly, it requires high investment for a long time (8-15 years) with uncertainty of several aspects such as: positive outcome of the antigen (risk on R&D), future demand (risk of no approval to commercialize or no inclusion in national immunization schedules), and profitability (depending on market's ability to pay off, competition and potential substitutes).

All those uncertainties translated for the manufacturers as risks, will be reflected in the *Conduct,* whereas the firms would expect higher returns to reward its risky investment (above of cost of production) and protect strongly its patents to ensure monopoly. Also, the biopharmaceutical companies would drive its resources to where are the greatest profit margins (mainly developing and supplying vaccines for diseases of HICs because their high ability and willingness to pay) and grouping its activities/plants in countries with highest tax benefits (such as tax exemption for R&D costs).

It is important to high-light that vaccine is not a recurrent use medicine as large part of the drugs, it is administered only once or twice in a lifetime of individuals, consequently the *Performance* of the industry would catch such peculiarity. The price elasticity, growth and profitability are limited by uncertain *Demand,* such as the seasonality of the disease, inclusion in the national vaccination agenda, coverage by health system (public or private), administration compulsoriness and eventual relaxation of IP (the CL) or new competitor. So, if in one hand the manufactures need to recover its long, risky and high investment mostly from a single dose with higher prices to keep the incentive to be in the market and invest further in new products, in the other hand it is held down by political and social claims of affordability and unfair profits of life-saving products.

Having in mind all those interconnections, the vaccine industry in Europe found out concentrated on *Demand* side because the Member-States are the main buyer to ensure the right to health to its citizens mainly through self-procurement methods – which by it turns is not the optimal instrument to capture lower prices due to smaller volume compared to collective purchase.

Further, the *Supply* side is as well concentrated, essentially in four large multinationals due to excessive barriers for new entries and low market incentives of return of investments. Accordingly, a low competition environment lacks the market force to push prices down, complementing the factor of high prices.

4.5 How can prices be lower?

The answer for the question of how it would be possible to lower the price of vaccines involves all of the complex cycle discussed in the present work, which is not intended to exhaustedly cover this subject, but to shed light on potential approaches. The relevant price elasticity should be the primary focus on the effect of high prices on public purchases, considering the bottleneck of financing R&D.

As R&D and manufacturing of vaccines are costly, risky and a lengthy process, the return on investment for the biopharmaceutical firms would be an intellectual property right protected by a patent to secure a period of time without competition and so rewarding these firms with a temporary monopoly. Such private financing model has led to the discovery of thousands of health solutions. However, more voices are now speaking up, arguing that this is an inadequate model in public health matters (PA, 2015; Mcguire, 2003; Miller, 2002; Rappuoli *et al* 2002), with fears that nothing less than a change to the capitalist underpinnings of the biopharmaceutical industry will resolve vaccine unbalance (Garretti, 2017, para 10).

The pool-procurement mechanisms mentioned in section 4.3.3 have obtained greater deals compared with self-purchases, but it is not the most diffused method of purchase in the EU, likely due to nationalic prerogatives of autonomy. Although it is important to mention a path towards greater collaboration in EU, such as: i) BeNeLuxA[3], which has been gradually exchanging sensitive pricing information between the members in a called "controlled transparency" and proposing joint determination of price range based in member's willingness to pay be shared publicly in advance of a bid with facultative choice by the countries to purchase or not (EPHA, 2019, pp.16-19); ii) the Valletta Declaration[4], a collaboration that one of its goals is joint negotiations and executing practices on pricing and reimbursement between the members (Rauland, 2020, p.1). To gain the economic advantages of volume purchase, the EU may need to change their framework from national to converge into a European Health Union.

[3] Beneluxa is an inter-government pharmaceutical policy initiative involving health services launched in 2015 in Belgium, the Netherlands, Luxembourg, Austria and Ireland (EPHA, 2019, p.1).
[4] Valletta Declaration was lunched in 2017 and countries participating are Cyprus, Greece, Ireland, Italy, Malta, Portugal, Romania, Spain, Slovenia and Croatia. (Rauland, 2020, p.1).

One of the potential ways to finance R&D would be the creation of an international global fund to pursue public health goods, a proposition of Archibugi and Bizzarri (2004) which would coordinate research agendas to promote preventive immunization for pandemics and neglected diseases – normally out of private market agenda. Such funds could finance the intellectual property or also buy the patents. Important to point out that some initiatives towards this solution are already existing such as the Coalition for Epidemic Preparedness and Innovations (CEPI), Bill & Melinda Gates Foundation and Wellcome Trust which supports significantly the R&D on vaccines not covered by regular market incentives (Bloom *et al.,* 2020, p.55).

Advance Market/Purchase Commitments (AMCs/APCs) would play a role sponsoring future purchases of certain quantities of vaccines at a specific price when the development of a new vaccine is in its final phases (Berndt *et al*, 2005 and Barder *et al*, 2006).

Another alternative to enhance lower prices through risk and expertise sharing could be the Product Development Partnership (PDP), normally a collective form aggregating the private and public sectors, non-profit organizations, and academia to advance the creation of a new product where commercial incentives are low. According to a study for Tuberculosis vaccine (Bessa *et al*, 2013) which assessed the PDP:

> "Promising research conducted at universities and public research institutions faces challenges in advancing the development of new vaccines due to high cost and the need for specialized capabilities to carry out the steps crucial to achieving licensed technologies. Public-private partnerships, including PDPs, have emerged as an alternative to join nonstate actors and for-profit and nonprofit organizations in less-hierarchical and less-bureaucratic horizontal collaborations, combining government financing and public health priorities with the efficiency and expertise of the private sector." (pp.4-5).

An example of the use of PDP is the Malaria vaccine (RTS,S), an initiative that united GSK, PATH Malaria Vaccine Initiative (MVI), with additional financial support of the Bill & Melinda Gates Foundation. The Malaria disease has been a great burden in the world with 214 million of cases per year and a challenging product formulation design to obtain efficacy; it has been under development for 28 years, and such long and risky context would not make the vaccine attractive for private market alone (AMF, 2017, pp.26-27).

Other alternatives to flexibilize pricing include adapting the product profile to be used under limited resources, such as multivalent vaccines, single doses, temperature stabilization, etc. Those initiatives would reduce the complexity of the use of the immunizing agents in the real world and reduce costs by simplifying stockage, storage, distribution and administration for several stakeholders.

In addition, there are discussions regarding the model of patents currently in existence and its use for strategic purposes by biopharmaceutical companies such as means for entry deterrence,

blocking competition instead of its original conceptual design, which was to reward innovation (Marengo, 2020, pp.516-517). However, eventual waive of IP would trigger the free rider problem, decreasing the incentive to invest in promising vaccine candidates and new technologies (Bloom *et al*, 2020, p.56).

The WHO (2021) already informed that the entry of new suppliers is helping to lower vaccines prices:

> "The entry of emerging market manufacturers, particularly in the underused vaccines market, has resulted in lower vaccine prices due to increased competition and higher production capacities for individual vaccines. A few emerging market manufacturers are also trying to expand their production to newer vaccines." (para 3).

In conclusion, on the whole, in the free market model, there is an assumption that all parties of an economic transaction are well informed to respond to price, thus individuals will determine the value ascribe to a good. But two questions are pertinent: i) Should health be considered a regular commodity? There is social disapproval of treating them as marketable because it is a fundamental right for all citizens and not a privilege for a few able to pay high prices. Vaccines are a cornerstone of a cost-efficient healthy system, adding unmeasured value to the society over decades. ii) Are the consumers well informed? There are blurred elements in pricing setups not disclosed by the manufacturers, so perhaps more transparency could play a role lowering prices - that is what will be investigated in the further chapter.

5. Pricing transparency

Expenditure in health represents a large part of the public budget in Europe, as the increasing constraints to balance revenue and spending pressures the national governments to be more efficient when managing public funds. In this context, it has never been so pertinent the saying of Benjamin Franklin: “an ounce of prevention is worth a pound of cure”. Vaccines are one of the most cost-efficient health commodities; it can prevent death and complications of several diseases, avoid the necessity of most expensive health treatments or even usage of social insurance resources, and potentially improve macroeconomic performance (Bloom *et al*., 2020, p.56).

Reliance on immunization tools control infectious diseases demands expressive expenditure on R&D, manufacturing and distribution capacity in a market-driven structure, culminating in high prices of vaccines in Europe. Moreover, there is a significant variance between minimum and maximum prices paid for the same product (WHO, 2017b, p.4), which suggests that there is space to achieve lower prices. Consequently, as price is considered one of the factors preventing the adoption of a vaccine in national schedule agendas, lower prices would mean more accessibility to society, and a decreased health budget burden while increasing the health of the population.

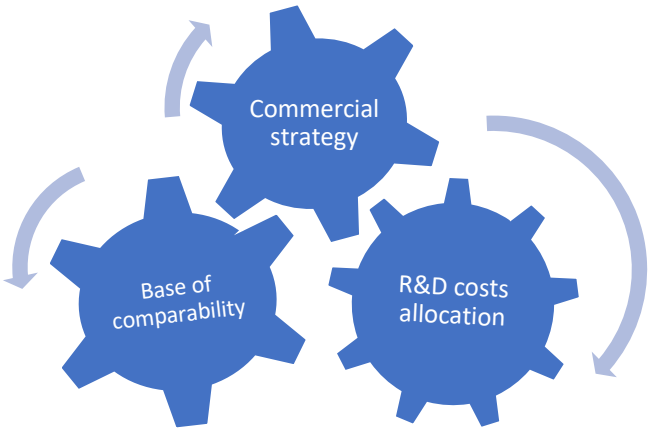
Accordingly, it is important to understand whether more transparency in the public disclosure of prices paid by public purchasers and key strategic pricing elements by the sellers would influence the market dynamics mitigating the effects of the information asymmetry to a certain extent to lower the prices of the vaccines in the EU.

WHO/UNICEF stated that the pricing of vaccines is considered less transparent among other life saving commodities (2015, p.1). It is important for the public health agents to understand the dynamics of the real costs of bringing vaccines to market for conscious decision-making, but the lack of disclosure of prices is a grey zone driven not only by the manufacturer but ironically as well by the public purchasers.

The main hazy pricing elements considered not transparent were enumerated by the WHO in the 2017 Fair Pricing Forum, as follows: i) lack of transparency on R&D via private and public funding; ii) lack of transparency of production costs and profit margins; iii) lack of transparency of the actual prices paid vs published prices (WHO, 2017c, p.6-7).

However, there are barriers to shedding light on this pricing information firstly, technical inabilities to determine how much of R&D costs were spent exactly on a specific vaccine project or directly associated with public funding for a specific outcome, as well as some vaccines that could benefit indirectly from discoveries and technologies from other projects. Secondly, the non-willingness to open strategic commercial information; thirdly, lack of comparable basis on prices eventually disclosed, driven by specific factors such as taxes, tariffs, logistic costs, subsidies, discounts and rebates applied.

Figure 5. 1 *Pricing transparency barriers for vaccines*



Note. The three main barriers of vaccine pricing transparency. Created by the author.

The need for greater pricing transparency is broadly recognized by the WHO. In May 2019 the WHO Assembly issued a resolution calling the countries to "take appropriate measures to publicly share information on the net prices of health products," (Fletcher, 2019, para 12) sending a clear push in favor of more clarity. But since 2020, with the Covid-19 pandemic, the pricing transparency on vaccines has captured more attention of society and the media, although this topic has been already raised by several institutions locally or globally for a long time, especially after the last H1N1 flu pandemic in 2008-2010.

The push to increase transparency was advocated by the WHO with an important milestone, which was the Global Vaccine Action Plan (GVAP) in 2012, where countries endorsed the request for more information on global-level prices as an effort to make viable more affordable vaccines and equitable prices for all, illustrated as follows:

> Monitoring GVAP progress, the WHO Strategic Advisory Group of Experts on immunization defined vaccine affordability as one of the five priority problems in GVAP implementation and called for a greater transparency in this are by encouraging countries to exercise more control on vaccine market and commit to sharing vaccine pricing information and working together to allow evidence-based assessment of the scale and scope of market imbalances, and allow solutions to be developed once problems are understood. (WHO/UNICEF, 2015, p.1).

The price for a vaccine varies for several factors related to its design, such as the type of antigen, technology used and distribution chain, but as well can vary due to the seller's strategy considering the country's GDP, volume and length of contracts and procurement method. So, a fundamental aspect to be developed is whether price transparency has a positive influence on affordability of vaccines in a sustainable way for both health systems and the biopharmaceutical industry and its reflections on accessibility of the right of health through higher society immunization.

5.1 Why is the transparency low?

According to an analytical paper conducted in 2021, the vaccine pricing in particular is influenced by a complex and frequently opaque give-and-take of private and public considerations (Neumann *et al.,* 2021, p.54). It is fundamental to understand why there is such low disclosure of pricing data and what are the power dynamics eventually preventing it.

The arguments by the biopharmaceutical firms regarding the non-disclosure of prices are mainly under the commercial strategy or a trade secret but seems that the real non-spoken reason is related to their possibility to exercise price discrimination on market segmentation freely, thus leveraging the firm's negotiation power and potentially leading to higher prices (EPHA, 2019, p.9).

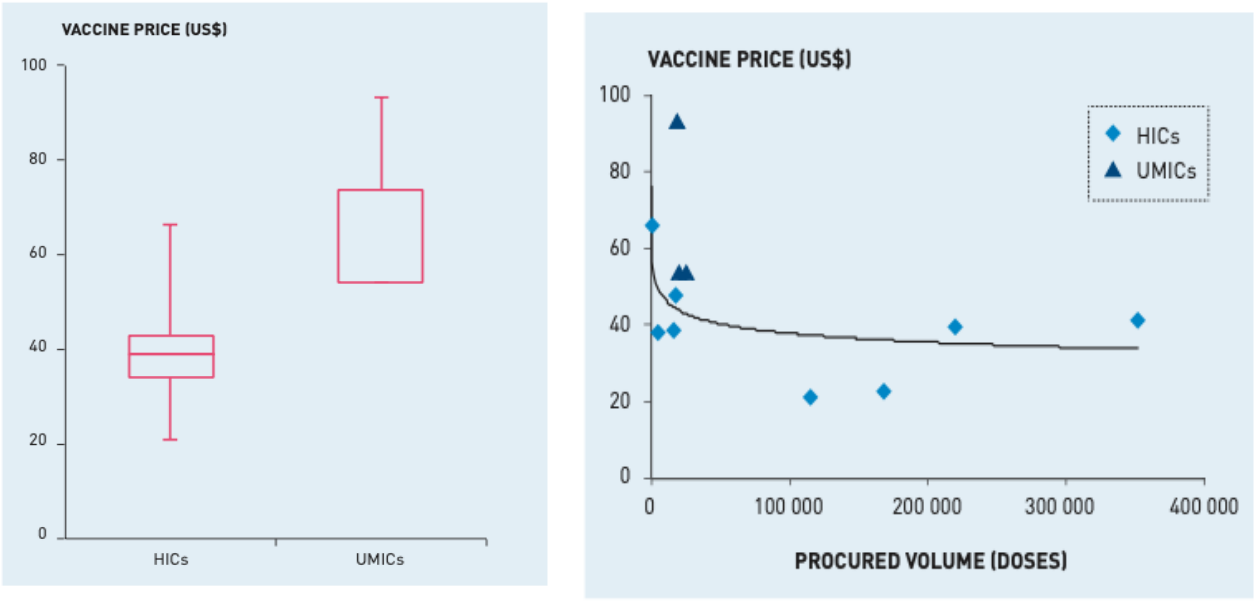
In theory, the principle of price discrimination is in line with price fairness since it justifies charging higher prices to the countries with more ability to pay (such as wealthier developed countries) while charging lower prices to the countries that cannot afford the price on the open market and for the donor supported procurement. This model weighs the benefits of adding a segment with the cost of the additional segment on consumers able to pay more, which maximizes the number of people benefited (more volume) and maximizes the revenue to the firm. Thus, it would be understandable that companies call for non-disclosure clauses in pricing to prevent wealthier countries from negotiating similar low prices as charged to low-income countries (LIC) and middle-income countries (MIC) (WHO, 2020, p.1).

Though, it is not a guarantee that LIC/MICs would effectively be charged relatively lower prices than HICs, especially if agreed prices are kept under contractual clauses of confidentiality.

To illustrate this discussion, a study from 2018 performed by Oxfam reveals that the profit margins by biopharmaceutical companies were similar in countries with stronger and lower purchasing power. This finding confutes the main argument used by health companies on charging HIC soaring prices because they profit less in poorer countries due to lower prices charged (Oxfam, 2018, p.9). Even if the above-mentioned report made by Oxfam is not only about the vaccine market because it also includes drugs, it provides a counterpoint of recurrent arguments of the industry (which frequently commercialize both vaccines and drugs) on price differentiation.

Specifically making a counterpoint with a vaccine example, the WHO reported in 2013 higher prices for HPV vaccines in UMICs than in HICs even with UMICs purchasing more quantity, and the LICs did not report prices paid to integrate the database on that occasion. In 2013 the HPV vaccine was considered a new and underused product, so the flagrant unexpected higher price paid by countries with the lowest ability to afford it raised public concerns on equity and sustainability of vaccine prices (WHO, 2015, p.12-13).

Figure 5.1. 1 *HPV vaccine price and volume in 2013 by country income group*



Note. The median value, the 25–75-percentile (interquartile) range, as well as the minimum and maximum price values paid for HPV vaccine in 2013. Reprinted from Regional office for Europe of WHO. Retrieved on May 13th, 2021, p. 13, from https://www.euro.who.int/en/publications/abstracts/review-of-vaccine-price-data-submitted-by-who-european-region-member-states-through-the-whounicef-joint-reporting-form-for-2013-2015. Copyright 2015 by WHO. Reprinted with permission.

In the example of the HPV vaccine, the disclosure of prices is an important tool to understanding why less wealthy countries were not able to achieve at least the same or a lower price per volume compared to HICs. The pricing transparency would play a role addressing procurement inefficiencies in making the vaccines, especially new products, fairer and more affordable.

Disclosing the paid values for vaccines from the other extreme of the relationship - the purchaser's point of view, which in EU is mostly public buyers - the critical aspects are first: confidentiality clauses that block it; secondly, the unwillingness of countries to share pricing data.

There is not much literature available explaining the first aspect of why the European countries would accept to kept secret public interest information (prices paid for immunizing products), but an analysis made by the European Public Health Alliance (EPHA) for accessibility and affordability of medicines summarized the blurry dynamic between public and private concerning the health market, as follows:

For a very long time, pharma executives would tour European capitals and talk public authorities into signing secret deals with confidentiality clauses in exchange for so-called discounts (which in turn would be hard to verify due to the exact same secrecy provisions). The usual response, an integral element of their "divide and conquer" tactics, was "don't worry about the (high) prices, we will provide you with the tools and methods to pay us as long as you keep the final price confidential." (EPHA, 2019, p.16).

Thus, it seems that the Member-States perceived a gain by accepting the confidentiality on prices in exchange for financial advantages such as discounts, rebates or longer time to pay the liability. To a certain extent, the heterogeneity of the European health framework (mentioned with details in chapter 3) is favoring such conduct, since the primary responsibility is with their own budgets and expenditures, and they prioritize what is beneficial from their local healthcare perspective (Morgan *et al.,* 2017).

By ensuring that pricing remains secret, the suppliers maintain their upper position over government negotiators who do not know what other countries are paying for the same product. Some biopharmaceutical companies even reinforce confidential protection by including clauses that allow them to suspend deliveries if countries reveal the price (Apuzzo and Gebrekidan, 2021, para 19).

Additionally, discussions of focus groups involved in the pharmaceutical segment revealed that policy makers and purchasers frequently report feeling pressured to accept unfavorable conditions and prices because of the need for quick access to new medicines for their patients (Vogler and Paterson, 2017, p. 146).

During the recent Covid-19 pandemic the flagrant exercise of power by the vaccine supplier over countries became evident in their negotiations in the confidentiality of pricing elements. In end of January 2021, members of the European Parliament read the first publicly available contract for purchasing coronavirus vaccines, but fundamental information was redacted such as the price per dose and values being paid on up front delivery (EP, 2021,p.1; Apuzzo and Gebrekidan, 2021, para 1).

Such asymmetry bothered society, including politicians, and leaks of prices and contracts occurred, like in the Twitter account of the Belgium Health Minister Eva De Bleeker in December 2020 regarding the prices of 6 to 7 vaccines in the European Commission's portfolio (Boseley, 2020); and in 2021 contracts with Pfizer-BioNTech were published in the media, revealing the upfront payments agreed (Reuters, 2021).

Those leaks brought light into the shadowy area, which is the market power of the supplier, and onto the incoherence of arguments when justifying the pricing variations that do not necessarily reflect the economic situation of the purchasing country. For instance, the New York Times disclosed that South Africa paid double (USD 5.25) for the Covid-19 vaccine produced by

AstraZeneca/University of Oxford than the EU countries (USD 2.19) agreed to pay per dose (Apuzzo and Gebrekidan, 2021).

Corroborating to deconstruct the argument that sustains the secrecy on pricing, Fatima Suleman informed that:

> "This idea of don't tell your price because you are getting the best price and no one else is getting that price is actually not true. African countries have been held to these non-disclosure agreements many times before believing that they are getting the best price, and then they learn that wealthy countries are actually getting lower prices than they are." (Tomlinson, 2021, p.1).

Moreover, not only companies and countries received claims for more data disclosure in the pandemic. An important global partner in the vaccine field, CEPI was as well. The coalition had raised 1.4 billion dollars in support of COVID-19 vaccine R&D and such a soaring amount raised flags for more accountability and transparency. Relevant information to society such as inclusion of *public health licence* clauses in the 3 largest agreements (with Novavax, AstraZeneca and Clover) was disclosed publicly one year later. The sharing of such clauses is important because it can change the market dynamics, in consequence, the price of pandemic vaccines. If the original manufacturer does not fulfil their equitable access commitments, CEPI could access intellectual property that arise from its funding and use a third part to produce the vaccine (Usher, 2021, pp.265-266).

Equally important to mention is that there are many contracts between biopharmaceutical and countries without non-disclosure clauses and still the pricing outcome is not publicly disclosed to society. According to the WHO/UNICEF, the vaccine pricing information is feasible in European countries, but the data is hardly available or published by them (WHO/UNICEF, 2015, p.4).

In Europe, a milestone towards more transparency was the Joint Reporting Form (JRF) done in 2014 under coordination of the WHO and UNICEF, which collected data in 2013 from 47 of 53 European countries creating a framework of regional vaccine data, aiming to empower countries for decision making and assisting health budgeting experts to improve the efficiency of vaccine procurement. Even though the database generated had limitations on its comparability (e.g., prices reported using different parameters), and WHO's recommendation was to not use the prices published as benchmarks, as it was already a great step towards more public vaccine pricing data. A briefing on vaccine pricing information provided by the JRF grouped by countries' income:

Figure 5.1. 2 *Availability and transparency of vaccine pricing information in 2013 by country income group in Europe*

Country income group (no. of countries)	Vaccine price information								
	Available at national level			Published in public domain			Restricted by legal provisions		
	Yes	No	Total no. of answers	Yes	No	Total no. of answers	Yes	No	Total no. of answers
HIC (33)	11	6	17	4	12	16	3	13	16
UMIC *(12)*	5	2	7	3	2	5	0	5	5
LMIC *(6)*	3	0	3	2	1	3	0	3	3
LIC *(2)*	2	0	2	0	1	1	0	2	2
Total (53)	21	8	29	9	16	25	3	23	26

Note. European countries reporting vaccine price information in the JRF. Reprinted from the Regional office for Europe of WHO. Retrieved on 10th May, 2021, p. 4 from https://www.euro.who.int/en/publications/abstracts/review-of-vaccine-price-data-submitted-by-who-european-region-member-states-through-the-whounicef-joint-reporting-form-for-2013-2015. Copyright 2015 by World Health Organization. Reprinted with permission.

From the results consolidated above for Europe, it is possible to state that the vaccine price information is available at the national level (21 out of 29 reporting countries). But the willingness to share the data was relatively low, only 36% (9 out of 25 reporting countries) published its vaccine pricing. Only 3 countries reported restrictions on data disclosure: one case specifically by legal provisions; two others referred to a current practice of keeping the data confidential.

Those results could seem paradoxical as previously were argued on the push from firms to restrict the disclosure of pricing data, but it is important to have in mind when observing this figure: i) the limited number of countries that fully replied the WHO/UNICEF survey in 2013 for the European region: about 50% replied of the universe of European countries reporting (53 countries)[5] and relevant countries did not report at all, such as Germany, France and Belgium; ii) the survey question that triggered the field "restricted by legal provisions" was not set up by a specific type of vaccine[6]; iii) today there are more vaccines available on the market than 8 years ago (such as Zoster, HPV and Covid-19).

To summarize, the discussion around the low transparency of vaccine price inputs is mainly embedded in mechanisms for increasing bargaining power. Evidence from several real-life cases and economic theory suggests that price transparency enhances informed decisions and negotiating positions of purchasers (Vogler and Paterson, 2017, p 147). In general, authors suggested that Member-states do not realize their own bargaining power as buyers and

[5] Just to illustrate to put into another perspective: the total number of countries that replied the WHO/UNICEF 2013 European survey represents 13% of the totally of countries that the UN recognizes (195 countries); 25% is the European proportion (53 countries of 195) on total number of countries recognized.

[6] The mentioned question in the survey was stated as: "Are there legal provisions restricting sharing information on prices of vaccine, procured for the national immunization programme, in your country? If yes, please provide details on provisions that do restrict sharing vaccine price information."

investors, and how those countries are missing opportunities to negotiate more effectively by sharing pricing information and joining collective pool-procurement purchases (WHO, 2017c, p.4) to make vaccines more accessible.

5.2 Would more transparency lower the vaccine price?

The current section aims to analyze whether sharing vaccine price publicly would lower the prices potentially through enhancing the competitiveness, facilitating symmetric negotiations, and building bridges to fairer and affordable prices, cascading effects to a greater immunization reach.

For the above-mentioned goal it is relevant to make a distinction in the prices referred to; the most relevant information would be the net prices paid per individual dose because of the comparability basis. In other words, the value per vaccine dose not including logistic costs, taxes, tariffs, discounts or rebates, because those rubrics are not related to the market power of the suppliers and net prices offer a better base of comparison between countries or buyers.

There are not many conclusive studies on correlations between transparency and pricing in the health industry (Vogler and Paterson, 2017, p. 147), eventually because of non-disclosure clauses preventing researchers from assessing prices. The WHO recognized this lack of scientific confirmation in a report of 2018, as follows:

> "Theoretical arguments on whether greater price transparency would lead to higher or lower medicine prices are inconclusive. There is a lack of evidence of the effectiveness of confidential agreements in lowering prices and improving access. On the other hand, **there is limited context-specific evidence that improving price transparency has led to better price and expenditure outcomes** (emphasis added). Nonetheless, improving price transparency should be encouraged on the grounds of good governance." (WHO, 2018b, para 37)

Although there is a limited number of scientific works in health to enrich the current line of argumentation (especially if niched to vaccine), the presence of evidence that more transparency improves the price lowering spent in specific context (such as off-patent health therapies) is still high-lighted (WHO, 2018b; WHO, 2020; Berdud *et al*., 2019).

Either way, relying on the positive contribution of a better governance through public transparency on the prices allows society to demand more accountability of a country's expenditure. Perhaps having more oversight, the country has the momentum to improve public procurement tools by a lean process (less discretionary with clear rules), more efficient negotiations or even lower incentives for corrupt behavior.

5.3 Arguments against and in favor of pricing transparency lowering vaccine price

Some authors advocate that more transparency would not decrease prices recurrently, such as Kal, Annemans and Garrison (2013). According to them, in the short term, it would achieve lower prices, but in the long term, more disclosure might set price convergence at the higher level because of the manufacturers reluctance to launch products at a lower price in a LIC – which set the average prices higher. Eventually, it would increase the inequity of access for poorer countries and worsen the incentive to innovate health therapies in a global marketplace (p. 738).

Furthermore, another negative effect of pricing transparency mentioned by other authors (Levenstein and Suslow, 2006; Albæk et al., 1997) is the possibility of easy collusion[7] on the part of the suppliers. When prices are fully disclosed, companies have more tools to maintain collusion given that it is easier for the rivals to detect any deviation of behavior agreed (Berdud, 2019, p.11).

On other hand, rebating this argument, the authors (Harrington, 2006; Porter 2005) suggest that it would be easier for the authorities to detect collusion practices because of the availability of its data, which can be investigated. Thus, in order to capture mainly positive effects of price disclosure, sensitive information (like the identity of the bidders) might be assessed if better off.

In contrast, other researchers encourage price disclosure, such as Vogler and Paterson (2017):

> "We encourage policy makers to implement collaborative action leading to a disclosure of actual prices paid. While this may cause some short-term 'pain' in terms of reduced industry willingness to offer discounted prices, we believe that the longer term 'gain' from reducing the information asymmetry and producing a more level playing field for negotiation between payers and industry would justify any short-term downside." (p. 147).

Follow the figure below to summarize the arguments of pricing transparency found in the literature review.

[7] For the OECD: "collusion refers to combinations, conspiracies or agreements among sellers to raise or fix prices and to reduce output in order to increase profits. As distinct from the term cartel, collusion does not necessarily require a formal agreement, whether public or private, between members. However, it should be noted that the economic effects of collusion and a cartel are the same and often the terms are used somewhat interchangeably." (OECD, 2021, para 1-2)

Figure 5.3. 1 *Arguments in favor and against vaccine pricing transparency*

In favor	Against
Short-term: higher prices (less discounts)	Short-term: lower prices
Long-term: lower prices	Long-term: higher prices
Higher symmetric pricing information	Higher inaccessibility to LIC
Balanced negotiation power	Lower incentive for health innovation
Easy to detect collusion	Easy collusion

Note. Table of main arguments used in favor and against the public disclosure of vaccine's price. Created by the author.

Important supra-national organizations engage the initiative to make public available vaccine's prices, such as UNICEF SD, PAHO RF, Médecins Sans Frontières Right-Shot, the GAVI and the WHO V3P (WHO/UNICEF, 2015, p.1). The WHO have an active role in the Global Vaccine Action Plan (GVAP) by monitoring global price and price transparency trends through the V3P platform – a tool which collects vaccine price information from countries and shares it online (WHO/UNICEF, 2015, p.18).

Despite WHO's great effort with V3P to coordinate the sharing of data of vaccine prices, researchers still are unable to fully make a conclusive analysis because of the limitations in its comparability. Illustrating this situation in 2017, Fadeyi, McLean, Tavella and Heron assessed seven vaccine (Rotavirus, HPV, PCV, Varicella, Yellow Fever, Influenza A, IPV) prices in 2014 and 2015 and concluded that the procurement process methods used by the countries were not transparent, jeopardizing a conclusive view on vaccine affordability and price impact broadly, as follows:

> Tiered-pricing or pooled procurement are methods employed by HICs or LICs to procure vaccines; however these processes are not transparent, so it is difficult to determine the vaccine price that should be set in different market. Further research to investigate the exact methods for vaccine price setting is needed, as well as a comprehensive review of vaccine affordability in LMICs and UMICs and how it impacts global vaccine pricing. (2017, para.3)

Moving forward, the literature review suggests that some authors make distinctions of transparency for health solutions protected by patents (on-patents) from others in which the IP already expired (off-patent). This division is justified because of the different results of price disclosure on them regarding the discriminatory or tiered pricing reflects in maximising access and rewards innovation.

A research paper of 2019 investigated the role of pricing transparency for medicines under such sub-division of patents, suggesting that:

i) On-patents: price transparency is not recommended to lower prices. In the lack of global agreement on tiered pricing by region and market, the disclosure result will slow the diffusion of innovative products to LIC and so reduces access to health solutions. (Berdud *et al*., 2019, p.24)

ii) Off-patents: price transparency is recommended only between buyers among themselves. It could improve market efficiency, thereby attracting more suppliers through price sensitivity (from difference of real and quality perceived of products by the buyers). (Berdud *et al*., 2019, p.22-23)

The market dynamics in the off-patent health products are more elastic due to the higher competition environment versus the monopolistic environment. In the EC panel of experts in 2015, it was equally confirmed: "In pharmaceutical markets, competition in generics has been able to provide wider access at lower prices in several EU countries" (EXPH, 2015, para 254).

To conclude, vaccines are considered by many authors as the cornerstone of a modern healthy society and multiple stakeholders share the responsibility for ensuring all citizens can benefit from it, as health is a fundamental right. Through literature review still inconclusive the empiric role of price transparency in the vaccine's market dynamics, likely caused by historical non-disclosure of this data as just recently in 2014 public initiatives were launched lacking more factors to allow comparability. Arguments around the correlation between price and transparency mentioned by authors pointed towards balance in negotiation power, information asymmetry, level of prices on poorer consumers, level of competition and cooperation among countries.

The Brazilian historian, Leandro Karnal, summarized that in the history of the humanity three events accelerated our evolution: war, technological revolution and epidemics (CNN, 2020), leading to more significant advance for society after such down-graded periods. In an optimistic way of thinking, the crescent and exponential importance that immunization policies gained throughout 2020 with the Covid-19 outbreak combined with the huge use of mRNA technology may promote the necessary push to rethink the market dynamics to boost transparency and accessibility of vaccines for society in the future.

6. Conclusion

This research aimed to analyze if more transparency in vaccine (net) pricing through public disclosure would i) increase the perception of price fairness and ii) lower prices, causing more accessibility of vaccines to society through non-systematic literature reviews and analytical frameworks (SCP paradigm).

For the first hypothesis, it was concluded that more disclosure of prices may increase the perception of fairness to buyers as they would be able to be well-informed on pricing differences between the available sorts of vaccines and they will have baselines to better perceive price variations. More transparency would help to offset the downgrade of fairness in eventual price increases not caused by higher profit margins such as unplanned costs or supply disruptions. Also, more disclosure may support to balance asymmetric information, especially in monopolistic/oligopolistic industries and in a market closely involved with fundamental rights such as health, in which consumers expect a level of altruism from companies to perceive a price as fair.

The second hypothesis was inconclusive as to whether more transparency would induce vaccine prices to be cheaper. The literature review suggests that authors may segregate the transparency effect of health products which are protected by patents (on-patents) or not (off-patent). Such division in the analysis is justified because of the different results of price disclosures on distinct market dynamics; off-patent health products are more elastic due to the higher competition environment versus the limited elasticity of the on-patent products, which is common under a monopoly or oligopoly. Therefore, authors suggest that more transparency on prices may decrease prices for off-patent vaccines while on-patent vaccines would not experience the same effect.

These conclusions were made through the support of three relevant research questions, summarized below:

i. Why do fair prices matter? Because health is a fundamental human right; when citizens are in good state of well-being they can utilize all other rights. Guaranteeing the access to life-transforming health commodities such as vaccines, on a trend of increased prices, is a challenge for a nation's budget and can impact a country's decision on the adoption of a vaccine in its immunization agenda.

ii. Why are prices high? With support of the SCP paradigm, the findings indicated that high prices were driven by the competitive environment with market concentration on supply (mainly four large multinational manufacturers) and demand (mostly public purchasers self-procuring to its own EU Member-State); presence of extensive and heterogenic regulation (national and EU policies); and high operational barriers to entry of new suppliers.

In a nutshell, the vaccine business has a complex process: the research, development and manufacture of a vaccine is costly (R&D estimated in USD 200-500 million and manufacturing facility in a range between USD 500 million to USD 1.5 billion), risky (uncertainty of a successful commercialized product reaching the minimum efficacy/ safety levels, uncertainty of approval by regulatory authorities, and uncertain demand of consumption) and long (about 8-15 years). On top of this, a vaccine is not a recurrent medical solution, since and individual normally takes a vaccine for a specific disease only once or twice in his life, a fact which limits the consumption demand compared with other health products. These barriers promote the elements to keep prices high because, under the market's dynamic, the greater risks taken by firms must be rewarded by a higher return (higher profit margins), thus generating the market incentives for companies to stay in the business and develop new vaccines.

iii. Why is transparency in price disclosure low? Mainly because of the interests involved to keep it non-disclosed publicly. Authors informed that buyers (mainly the governments) agree to keep prices secretly in exchange of financial benefits such as higher discounts, rebates or longer payment terms. The firms insist to not disclose prices to be able to make price discrimination in the different segments without public scrutiny, which often leverages their negotiation power.

As it can be seen, despite the high value for the humanity of vaccination against communicable diseases over the decades (especially recognized in pandemics), economical aspects create challenges for achieving socially optimal levels of vaccine R&D, production, and uptake.

The challenges of setting vaccine prices are multifold: the need for constant updates to reflect changing economic circumstances and social expectations while ensuring a financial return for private investors (including shareholders), risks of shortages or stockpiling, and risks of falling afoul of antitrust laws due to excessive regulation. Most importantly, health should be seen as an outcome of one partner alone: sustainable and equitable improvements in health are the product of effective policy across all parts of governments and collaborative efforts across all stakeholders in the cycle of a vaccine from the R&D until it reaches the final user. The pricing transparency could be an instrument to enhance the competitiveness, facilitate symmetric negotiations, and build bridges to fairer and affordable prices, cascading effects to a greater immunization for society.

Nevertheless, the current thesis faced limitations on finding qualitative or quantitative research material mainly driven by the nature of the topic remaining confidential (e.g. vaccine prices and its composition) and when available, it is often displayed on a basis which a comparison or correlation analysis would not be effective. This constraint rendered the second hypothesis proposed in the current thesis to be inconclusive.

Finally, some recommendations proposed to increase transparency in vaccine pricing and to promote fairer and lower prices are enumerated below:

By Governments and European institutions:

- Increase the use of pooled-procurement mechanisms within EU
- Improve efficiency of procurement tools based on regular performance assessment findings with greater collaboration between European countries
- Support vaccine pricing transparency efforts regionally and globally through increased information-sharing of prices and its elements on comparable bases publicly and regularly, including their contribution in R&D
- Realign market incentives for R&D of new and innovative vaccines and exploring new models of funding it
- Build a path for a health union in the EU centralizing and harmonizing the regulatory and reimbursement aspects.

By manufacturers:

- Disclosure of the actual amount spent on R&D and production publicly, per product
- Publish their complete pricing strategy for all vaccines per market
- Disclosure of the firm's tax practices (e.g. country-by-country report and list of subsidiaries in operational countries) and values received as subsidies or tax exemption per country

By developing this academic research in which qualitative data was catalyzed, there is a hope that it can contribute to inform other researchers about the key elements related to vaccine pricing and transparency, and to build a path for more quantitative and real case based-evidence investigations in this critical and underserved field.

Bibliography

Access to Medicine Foundation. (2017). *Access to Vaccines Index 2017*. https://accesstomedicinefoundation.org/access-to-vaccines-index/results

Albæk, S., Møllgaard, P., & Overgaard, P.B. (1997). *Government-Assisted Oligopoly Coordination? A Concrete Case*. The Journal of Industrial Economics, 45, 429-443. https://doi.org/10.1111/1467-6451.00057

Apuzzo, M., & Gebrekidan, S. (2021, January 28). Governments Sign Secret Vaccine Deals. Here's What They Hide. *New York Times*. https://www.nytimes.com/2021/01/28/world/europe/vaccine-secret-contracts-prices.html

Archibugi, D., & Bizzarri, K. (2004). Committing to vaccine R&D: a global science policy priority. *Research Policy*, 33(10), 1657–1671. https://doi.org/10.1016/j.respol.2004.10.003

Bain, J. S. (1969). Industrial Organization. Second edition. New York, London, J. Wiley & Sons, Inc., 1968, XIV p. 678 p., 97/—. (1969). *Louvain Economic Review*, 35(3), 225-225. doi:10.1017/S077045180004207X

Barder, O., Kremer, M., & Williams, H. (2006). *Advance market commitments: a policy to stimulate investment in vaccines for neglected diseases*. Economists' Voice, The Berkeley Electronic Press.

Bassani, D. G., Arora, P., Wazny, K., Gaffey, M. F., Lenters, L., & Bhutta, Z. A. (2013). Financial incentives and coverage of child health interventions: a systematic review and meta-analysis. BMC public health, 13 Suppl 3(Suppl 3), S30. https://doi.org/10.1186/1471-2458-13-S3-S30

Beckert, Jens. (2011). Where Do Prices Come From? Sociological Approaches to Price Formation. *Socio-Economic Review*, 9(4), 757–786. https://doi.org/10.1093/ser/mwr012

Berndt, E. R., Bir, A., Busch, S. H., Frank, R. G., & Normand, S. L. (2002). The medical treatment of depression, 1991-1996: productive inefficiency, expected outcome variations, and price indexes. Journal of health economics, 21(3), 373–396. https://doi.org/10.1016/s0167-6296(01)00132-1

Berndt, E. R., Glennerster, R., Kremer, M. R., Lee, J., Levine, R., Weizsäcker, G., & Williams, H. (2007). Advance market commitments for vaccines against neglected diseases: estimating costs and effectiveness. *Health economics*, 16(5), 491–511. https://doi.org/10.1002/hec.1176

Bessa T. C. B. *et al*. (2017). R&D in Vaccines Targeting Neglected Diseases: An Exploratory Case Study Considering Funding for Preventive Tuberculosis Vaccine Development from 2007 to 2014. *BioMed Research International*. https://doi:10.1155/2017/4765719

Blank, P. R., Schwenkglenks, M., Sardos, C. S., Patris, J., & Szucs, T. D. (2013). Population access to new vaccines in European countries. Vaccine, 31(27), 2862–2867. https://doi.org/10.1016/j.vaccine.2013.04.039

Bloom, D., Cadarette, D. & Tortotice, D. (2020). *An Ounce of Prevention - Our approach to vaccine finance is ill-suited to addressing epidemic risk*. International Monetary Fund. https://www.imf.org/external/pubs/ft/fandd/2020/09/vaccine-finance-epidemics-and-prevention-bloom.htm

Boseley Sarah. (2020, December 18). Belgian minister tweets EU's Covid vaccine price list to anger of manufacturers, *The Guardian*. https://www.theguardian.com/world/2020/dec/18/belgian-minister-accidentally-tweets-eus-covid-vaccine-price-list

Bright, K.; Kiewell, D. & Kincheloe, A. (2006) *Profiting from proliferation.* McKinsey & Company, pp.75-83.

CNN. (2020, April 18). CNN Brazil. https://www.cnnbrasil.com.br/nacional/2020/04/19/mundo-pos-pandemia-vivera-periodo-de-grande-alegria-e-felicidade-diz-karnal

Cutler, David, Mark McClellan, Joseph P. Newhouse, and Dahlia Remler. (2001). *Pricing Heart Attack Treatments*. University of Chicago Press, 305-362. https://doi.org/10.7208/9780226132303-010

Daems, Rudi. (2008). *Medicines for the developing world.* Universitaire Pers Maastricht. ISBN 978 90 5278 790 9

Drummond, M. (2007). NICE: A nightmare worth having? *Health Economics, Policy and Law*, 2(2), 203-208. https://doi.org/10.1017/S1744133107004033

Dyakova, M.; Hamelmann, C.; Bellis, M. A., Besnier, E., Grey, C.N.B.; Ashton, K *et al*. (2017). *Investment for health and well-being: a review of the social return on investment from public health policies to support implementing the Sustainable Development Goals by building on Health 2020*. WHO Regional Office for Europe. https://www.euro.who.int/__data/assets/pdf_file/0008/345797/HEN51.pdf

Elbe, S., Roemer-Mahler, A., & Long, C. (2014). Securing circulation pharmaceutically: Antiviral stockpiling and pandemic preparedness in the European Union. *Security Dialogue*, *45*(5), 440–457. https://doi.org/10.1177/0967010614530072

European Centre for Disease Prevention and Control. (2021). COVID-19 situation update worldwide, as of week 18, updated 12 May 2021. https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

European Commission. (2015). Expert Panel on effective ways of investing in Health (EXPH), *Report on Investigating policy options regarding competition among providers of health care services in EU Member States*. https://doi:10.2875/867590

European Commission. (2015). *European Semester Thematic Fiche: Health and Health systems.* https://ec.europa.eu/info/business-economy-euro/economic-and-fiscal-policy-coordination/eu-economic-governance-monitoring-prevention-correction/european-semester_en

European Commission. (2018). *Strengthened Cooperation against Vaccine Preventable Diseases*. COM(2018) 245, Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee Of The Regions.

European Commission. (2018). *Vaccination Programmes and Health Systems in The European Union* - Report of the Expert Panel on Effective Ways of Investing In Health, European Union, pp. 12 and 43-44. https://doi:10.2875/18503

European Commission. (2019). Memo 28/03/2019, *Framework contracts for pandemic influenza vaccines.* https://ec.europa.eu/health/sites/health/files/preparedness_response/docs/ev_20190328_memo_en.pdf

European Commission. (2021). *Health security and infectious diseases*. https://ec.europa.eu/health/security/preparedness_response_en

European Health Forum Gastein. (2020). *Pharmaceutical Strategy for Europe: Building a comprehensive pharmaceutical policy to address today's challenges and tomorrow's realities.* Organised by the Directorate-General for Health and Food Safety of the European Commission. Conference Report 30 September – 2 October 2020. https://www.ehfg.org/documents/EHFG2020/Conference-Report/index_30.html#page=48

European Medicine Agency (EMA). (2009a). *CHMP assessment report on Novel Influenza (H1N1) outbreak Tamiflu (oseltamivir) Relenza (zanamivir)* https://www.ema.europa.eu/en/documents/other/chmp-assessment-report-novel-influenza-h1n1-outbreak-tamiflu-oseltamivir-relenza-zanamivir_en.pdf

European Medicine Agency (EMA). (2009b). *Pandemic report and lessons learned Outcome of the European Medicines Agency's activities during the 2009b (H1N1) flu pandemic* https://www.ema.europa.eu/en/documents/report/pandemic-report-lessons-learned-outcome-european-medicines-agencys-activities-during-2009-h1n1-flu_en.pdf

European Medicine Agency (EMA). (2020). *Human Regulatory Overview* https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines-development-evaluation-approval-monitoring

European Parliament. (1998). *Health care systems in the EU: a comparative study.* https://www.europarl.europa.eu/workingpapers/saco/pdf/101_en.pdf

European Parliament. (2011). *Differences in costs of and access to pharmaceutical products in the EU.* https://www.europarl.europa.eu/thinktank/en/document.html?reference=IPOL-ENVI_ET(2011)451481

European Parliament. (2021b, January 12). *COVID-19 vaccines: MEPs call for more clarity and transparency.* https://www.europarl.europa.eu/news/en/press-room/20210111IPR95308/covid-19-vaccines-meps-call-for-more-clarity-and-transparency

European Public Health Alliance. (2019). *Universal Access and Affordable Medicines-Beneluxa et al.: the best is yet to come.* https://epha.org/beneluxa-best-is-yet-to-come/

European Union. (2007, December 14). *European Union Charter of Fundamental Rights* https://fra.europa.eu/en/eu-charter/article/35-health-care

European Union. (2011) *Fact Sheets on the European Union.* https://www.europarl.europa.eu/factsheets/en/sheet/49/public-health

European Union. (2012). *The management of health systems in the EU Member States - The role of local and regional authorities*. https://doi:10.2863/83500.

European Union. (2019). *State of Health in the EU*, Companion Report 2019 https://doi:10.2875/85326

European Union. (2021). *Health Policy,* Overview and Priorities for 2016-2020. https://ec.europa.eu/health/policies/overview_en

Expert panel on effective ways of investing in health (EXPH) (2015). *Competition among health care providers - Investigating policy options in the European Union*. https://ec.europa.eu/health/sites/health/files/expert_panel/docs/008_competition_healthcare_providers_en.pdf

Fadeyi, I.; McLean ,T; Tavella, F. & Heron, L. (2017). Differences In Vaccine Pricing Between High-Income And Low-Income Markets*. Value in Health*, Volume 20 (9), p.411. https://doi.org/10.1016/j.jval.2017.08.080

Felter, C., Bussemaker, N., Persaud, S., & Speier, M. (2021). (Rep.). A Guide to Global COVID-19 Vaccine Efforts. *Council on Foreign Relations*. http://www.jstor.org/stable/resrep29817

Fletcher, Elaine R. (2019, May 28). World Health Assembly Approves Milestone Resolution on Price Transparency Medicines & Vaccines. *Health Policy Watch*. https://healthpolicy-watch.news/world-health-assembly-approves-milestone-resolution-on-price-transparency/

Friedman, M., & Friedman, R. D. (1980). *Free to choose: A personal statement*. New York: Harcourt Brace Jovanovich, 205-206. https://www.fdareview.org/features/quotations-economists-judgments-about-the-fda/

Galanakis, E., Jansen, A., Lopalco, P. L., & Giesecke, J. (2013). Ethics of mandatory vaccination for healthcare workers. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *18*(45), 20627. https://doi.org/10.2807/1560-7917.es2013.18.45.20627

Garretti, Laurie. (2017). *Inoculate against a global vaccine crisis*. Foreign Policy. https://foreignpolicy.com/2018/01/16/the-answers-are-out-there-natural-disasters-china-north-korea-corruption-economy/#health

Giuseppe, C.; Schwierz, C. & Xavier, Ana. (2012). *Cost-containment policies in public pharmaceutical spending in the EU*. European Commission Directorate-General for Economic and Financial Affairs. https://ec.europa.eu/economy_finance/publications/economic_paper/2012/pdf/ecp_461_en.pdf

Grabowski, H. G., & Vernon, J. (2000). The distribution of sales revenues from pharmaceutical innovation. *PharmacoEconomics*, *18 Suppl 1*, 21–32. https://doi.org/10.2165/00019053-200018001-00005

Greer, Scott. (2006). Uninvited Europeanization: Neofunctionalism and the EU in Health Policy. Journal of European Public Policy, 13, 134-152. https://doi.org/10.1080/13501760500380783

Harrington Jr. J.E. & Bos, A. M. (2013). *Competition policy and cartel size*. Maastricht University, Graduate School of Business and Economics. GSBE Research Memoranda No. 027 https://doi.org/10.26481/umagsb.2013027

Hendrix, K. S., Sturm, L. A., Zimet, G. D., & Meslin, E. M. (2016). Ethics and Childhood Vaccination Policy in the United States. *American journal of public health*, *106*(2), 273–278. https://doi.org/10.2105/AJPH.2015.302952

Huppertz, J., Arenson, S., & Evans, R. (1978). An Application of Equity Theory to Buyer-Seller Exchange Situations. *Journal of Marketing Research, 15*(2), 250-260. doi:10.2307/3151255

Institute of Medicine (US) Committee on the Evaluation of Vaccine Purchase Financing in the United States. (2003) *Financing Vaccines in the 21st Century: Assuring Access and Availability*. National Academies Press (US). https://www.ncbi.nlm.nih.gov/books/NBK221811/

International Monetary Fund. (2020). World Economic Outlook Database - EU October 2020. https://www.imf.org/en/Publications/WEO/weo-database/2020/October/weo-report?a=1&c=998,&s=NGDPD,PPPGDP,PPPPC,&sy=2019&ey=2025&ssm=0&scsm=1&scc=0&ssd=1&ssc=0&sic=0&sort=country&ds=.&br=1

Jennings, Katie. (2018, December 12). EU's health care tug of war. *Politico*. https://www.politico.eu/article/health-care-2024-eu-tug-of-war-medicines-medical-devices-tobacco-alcohol-vaccines/

Jorion, Paul. (2015). *Aristotles theory of price formation and views on chrematistics.* https://www.pauljorion.com/stewardship-of-finance/wp-content/uploads/2015/04/College-16-02-2015_Aristotles-theory-of-price-formation-and-views-on-chrematistics.pdf

Kahneman, D., Knetsch, J., & Thaler, R. (1986). Fairness as a Constraint on Profit Seeking: Entitlements in the Market. *The American Economic Review, 76*(4), 728-741. http://www.jstor.org/stable/1806070

Kaló, Z., Annemans, L., & Garrison, L. P. (2013). Differential pricing of new pharmaceuticals in lower income European countries. *Expert review of pharmacoeconomics & outcomes research*, *13*(6), 735–741. https://doi.org/10.1586/14737167.2013.847367

Karlin-Smith, Sarah. (2020, March 5). How the drug industry got its way on the coronavirus. *Politico*. https://www.politico.com/news/2020/03/05/coronavirus-drug-industry-prices-122412

Larson, H.J., de Figueiredo, A., Karafllakis, E., & Rawal, M. (2018). State of Vaccine Confidence in the EU. *European Commission*. https://doi:10.2875/241099

Lee, B. Y., & McGlone, S. M. (2010). Pricing of new vaccines. *Human vaccines*, *6*(8), 619–626. https://doi.org/10.4161/hv.6.8.11563

Levenstein, M., & Suslow, V. (2006). What Determines Cartel Success? *Journal of Economic Literature, 44*(1), 43-95. Retrieved May 20, 2021, from http://www.jstor.org/stable/30032296

Lipczynski, J., Wilson, J. O., & Goddard, J. (2009). *Industrial Organization: Competition, Strategy, Policy. 3rd Edition*. Prentice Hall.

Lo, A. W., Siah, K. W., & Wong, C. H. (2020). Estimating Probabilities of Success of Vaccine and Other Anti-Infective Therapeutic Development Programs. *Harvard Data Science Review*. https://doi.org/10.1162/99608f92.e0c150e8

Navin M. C. (2017). The Ethics of Vaccination Nudges in Pediatric Practice. *HEC forum: an interdisciplinary journal on hospitals' ethical and legal issues*, *29*(1), 43–57. https://doi.org/10.1007/s10730-016-9311-2

Mackenbach, J. P., Bakker, M. J., Kunst, A. E., & Diderichsen, F. (2002). Strategies to reduce socioeconomic inequalities in health. In *Reducing inequalities in health* (pp. 25-49). Routledge.

Maitland, I. (2002). Priceless Goods: How Should Life-Saving Drugs Be Priced? *Business Ethics Quarterly, 12*(4), 451-480. https://doi:10.2307/3857995

Marengo L. (2020). How much will the vaccine cost (if ever discovered….). *Journal of Industrial and Business Economics*, 1–7. Advance online publication. https://doi.org/10.1007/s40812-020-00166-7

Mcevoy, E., & Ferri, D. (2020). The Role of the Joint Procurement Agreement during the COVID-19 Pandemic: Assessing Its Usefulness and Discussing Its Potential to Support a European Health Union. *European Journal of Risk Regulation*, 11(4), 851-863. https://doi:10.1017/err.2020.91

McGuire T. G. (2003). Setting prices for new vaccines (in advance). *International journal of health care finance and economics*, *3*(3), 207–224. https://doi.org/10.1023/a:1025336903645

McKee, M., MacLehose, L.,& Nolte, E. (2004). Health Policy and European Union Enlargement. World Health Organization. ISBN 0335213537

McKinsey & Company. (2006). *Profiting from proliferation*. McKinsey & Company. 1, 131.

Médecins Sans Frontières. (2019, April 12). Humanitarian mechanism for vaccines used for first time in Europe to counter high prices. *MSF*. https://www.msf.org/humanitarian-mechanism-vaccines-used-first-time-europe-counter-high-prices

Médecins Sans Frontières. (2020, March 27). MSF calls for no patents or profiteering on COVID-19 drugs and vaccines. *MSF.* https://www.msf.org/msf-calls-profiteering-covid-19-drugs

Miller, H. (2002, August 19). An Indefensible Epidemic. *The Wall Street Journal*.

Morgan, S. G., Vogler, S., & Wagner, A. K. (2017). Payers' experiences with confidential pharmaceutical price discounts: A survey of public and statutory health systems in North America, Europe, and Australasia. *Health policy (Amsterdam, Netherlands)*, *121*(4), 354–362. https://doi.org/10.1016/j.healthpol.2017.02.002

Natsis, Yannis. (2018, July 11). The proposed European Commission Regulation on HTA: a golden opportunity for patients and health budgets. *European Public Health Alliance*. https://epha.org/proposed-ec-regulation-on-hta-golden-opportunity-for-patients-and-health-budgets/

Neumann, P. J., Cohen, J. T., Kim, D. D., & Ollendorf, D. A. (2021). Consideration Of Value-Based Pricing For Treatments And Vaccines Is Important, Even In The COVID-19 Pandemic. *Health affairs (Project Hope)*, *40*(1), 53–61. https://doi.org/10.1377/hlthaff.2020.01548

Nevel, Amy; Honeycutt, Amanda; Robinson, Tara; Layton, Christine. Influenza Vaccine Economics - Issue Brief. 2005. Accessed on 25 April 2021 on < https://www.rti.org/publication/influenza-vaccine-economics-issue-brief/fulltext.pdf>

Organisation for Economic Co-operation and Development. (2021). Glossary of statistical terms. Collusion. https://stats.oecd.org/glossary/detail.asp?ID=3159#:~:text=OECD%20Glossary%20of%20Statistical%20Terms%20%2D%20Collusion%20Definition&text=Definition%3A,in%20order%20to%20increase%20profits.

Our World Data. (2021, January 30). Vaccine Innovation. https://ourworldindata.org/vaccination

Oxfam. (2018). *Prescription for poverty - Drug companies as tax dodgers, price gougers, and influence peddlers*. https://www.oxfam.org/en/research/prescription-poverty

Parliamentary Assembly Council of Europe (PACE). (2010). Resolution 1749/2010: Handling of the H1N1 pandemic: more transparency needed. http://semantic-pace.net/tools/pdf.aspx?doc=aHR0cDovL2Fzc2VtYmx5LmNvZS5pbnQvbncveG1sL1hSZW

YvWDJILURXLWV4dHIuYXNwP2ZpbGVpZD0xNzg4OSZsYW5nPUVO&xsl=aHR0cDovL3NlbWFudGljcGFjZS5uZXQvWHNsdC9QZGYvWFJlZi1XRC1BVC1YTUwyUERGLnhzbA==&xsltparams=ZmlsZWlkPTE3ODg5>

Parliamentary Assembly. (2015). Resolution 2071. Public health and the interests of the pharmaceutical industry: how to guarantee the primacy of public health interests? http://semantic-pace.net/tools/pdf.aspx?doc=aHR0cDovL2Fzc2VtYmx5LmNvZS5pbnQvbncveG1sL1hSZWYvWDJILURXLWV4dHIuYXNwP2ZpbGVpZD0yMjE1NCZsYW5nPUVO&xsl=aHR0cDovL3NlbWFudGljcGFjZS5uZXQvWHNsdC9QZGYvWFJlZi1XRC1BVC1YTUwyUERGLnhzbA==&xsltparams=ZmlsZWlkPTIyMTU0≥

Paun, Carmen. (2019, December 4). Europe eyes arrival of world's priciest drug. *Politico.* https://www.politico.eu/article/europe-eyes-arrival-of-worlds-priciest-drug/

Paun, Carmen. (2016, September 30). Europe's health systems on life support. *Politico.* https://www.politico.eu/article/europe-health-care-systems-on-life-support-special-report-drug-pricing-medicines-public-services/

Pearl, Robert. (2019, June 10). The $2.1 Million Question: What Are the Medical, Ethical Implications Of The World's Priciest Drug?. *Forbes*. https://www.forbes.com/sites/robertpearl/2019/06/10/zolgensma-ethics/?sh=55659e5162bc

Pegurri, E., Fox-Rushby, J. A., & Damian, W. (2005). The effects and costs of expanding the coverage of immunisation services in developing countries: a systematic literature review. *Vaccine*, *23*(13), 1624–1635. https://doi.org/10.1016/j.vaccine.2004.02.029

Pentecost, Michael. (2006). Value-Based Competition in Health Care. Journal of the American College of Radiology, 3(10), 730 – 732. https://doi.org/10.1016/j.jacr.2006.07.003

Perry, Mark J. (2017). Health care is a commodity, not a right – and markets, not government are the solution in medical care. *AEI*. https://www.aei.org/carpe-diem/health-care-is-a-commodity-not-a-right-and-markets-not-government-are-the-solution-in-medical-care/>

Pöri, Pinja. (2018). *Development of Vaccines*. Metropolia University of Applied Sciences Bachelor of Engineering Biotechnology and Chemical Engineering. https://core.ac.uk/download/pdf/161424545.pdf

Porter, Robert H. (2005). Detecting collusion. Review of Industrial Organization, 26(2), 147-167. https://doi.org/10.1007/s11151-004-7294-7

Pritchett, L., & Summers, L. (1996). Wealthier is Healthier. *The Journal of Human Resources, 31*(4), 841-868. doi:10.2307/146149

Quilici, S., Smith, R., & Signorelli, C. (2015). Role of vaccination in economic growth. *Journal of market access & health policy*, *3*, 10.3402/jmahp.v3.27044. https://doi.org/10.3402/jmahp.v3.27044

Rangel E. K. (2008). Innovation and the Pharmaceutical Industry: Critical Reflections on the Virtues of Profit, H.T. Engelhardt, Jr. and J.R. Garrett (eds.) (Salem: M & M Scrivener Press,

2008). *HEC forum : an interdisciplinary journal on hospitals' ethical and legal issues*, *20*(4), 375–378. https://doi.org/10.1007/s10730-008-9085-2

Rappuoli, R., Miller, H. I., & Falkow, S. (2002). Medicine. The intangible value of vaccination. *Science (New York, N.Y.)*, *297*(5583), 937–939. https://doi.org/10.1126/science.1075173

Rauland, Marco. (2020). Cross Country Collaborations in Europe: The Future of Pricing & Access Negotiations?. *Pharma Board Room*. https://pharmaboardroom.com/articles/cross-country-collaborations-in-europe-the-future-of-pricing-access-negotiations/

Rawls, J. (1958). Justice as Fairness. *The Philosophical Review, 67*(2), 164-194. https://doi:10.2307/2182612

Rechel, B & Priaulx, Jennifer & Richardson, Erica & McKee, M. (2019). The organization and delivery of vaccination services in the European Union. *European Journal of Public Health*. 29. https://10.1093/eurpub/ckz185.375.

Rémy, V., Zöllner, Y., & Heckmann, U. (2015). Vaccination: the cornerstone of an efficient healthcare system. *Journal of market access & health policy*, *3*, 10.3402/jmahp.v3.27041. https://doi.org/10.3402/jmahp.v3.27041

Reuters. (2021, April 21). Leaked EU-Pfizer contract shows price for COVID vaccines set at 15.5 euros per dose. https://www.reuters.com/article/health-coronavirus-eu-pfizer-idUSL1N2ME0Z5

Rotemberg, Julio. (2011). Fair Pricing. *Journal of the European Economic Association*, 9(5). https://doi:10.2307/41305841.

Ruijter, Anniek de. (2019). EU Health Law & Policy: The Expansion of EU Power in Public Health and Health Care. https://doi:10.1093/oso/9780198788096.001.0001.

Sachs, Jeffrey. (2021, April 29). Share the Intellectual Property on COVID-19. *Project Syndicate.* https://www.project-syndicate.org/commentary/covid19-intellectual-property-waiver-is-a-moral-imperative-by-jeffrey-d-sachs-2021-04

Sandel, M. J. (2009). *Justice: What's the right thing to do?.* New York: Farrar, Straus and Giroux.

Sanofi. (2017). Understanding the complexity of vaccine manufacturing. https://www.sanofi.com/en/media-room/articles/2017/understanding-the-complexity-of-vaccine-manufacturing

Scherer F. M. (2001). The link between gross profitability and pharmaceutical R&D spending. *Health affairs (Project Hope)*, *20*(5), 216–220. https://doi.org/10.1377/hlthaff.20.5.216

Schlegelmilch, Bodo B. (1997). Marketing Ethics: An International Perspective. Thomson Learning, reproduced from article of Richard A. Spinello (1992), Journal of Business Ethics (11), 617-626.

Schoonackers, R. (2020). *Tax incentives for R&D: Are they effective?.* National Bank of Belgium. https://www.nbb.be/doc/ts/publications/economicreview/2020/ecorevii2020_h4.pdf

Singh, K., & Mehta, S. (2016). The clinical development process for a novel preventive vaccine: An overview. *Journal of postgraduate medicine*, *62*(1), 4–11. https://doi.org/10.4103/0022-3859.173187

Smith, T.J., (2012). *Pricing strategy*. Manson: South-Western Cengage Learning.

Stevens, Philip. (2007). *Fighting the diseases of poverty*. International Policy Press. ISBN 9781412807449

Sturcke, James & Bowcott, Owen. (2010, April 29). Drug companies face European inquiry over swine flu vaccine stockpiles. *The Guardian*. https://www.theguardian.com/world/2010/jan/11/swine-flu-h1n1-vaccine-europe

Thomson, S., Foubister, T. & Mossialos, E. (2009). *Financing health care in the European Union: Challenges and policy responses*. https://www.euro.who.int/__data/assets/pdf_file/0009/98307/E92469.pdf?ua=1

Tomlinson, Catherine. (2021, March 2). How do you price a life-saving vaccine during a pandemic?. *24hNews.* https://www.news24.com/news24/analysis/analysis-how-do-you-price-a-life-saving-vaccine-during-a-pandemic-20210303>

United Nations. (2020). *Universal Declaration of Human rights.* https://www.un.org/en/universal-declaration-human-rights/

United Nations High Commissioner for Human Rights and World Health Organization. (2020). *The right to health*, Fact Sheet No. 3. https://www.ohchr.org/Documents/Publications/Factsheet31.pdf

Usher, Ann D. (2021). CEPI criticised for lack of transparency. *The Lancet,* 397(10271), 265 – 266. https://doi.org/10.1016/S0140-6736(21)00143-4

Vaccines Europe. (2021). The EU Vaccine Industry in Figures. https://www.vaccineseurope.eu/wp-content/uploads/2020/02/VE_Factsheet.pdf

Vogler, S., Paterson, K.R.(2017). Can Price Transparency Contribute to More Affordable Patient Access to Medicines?. *PharmacoEconomics Open,* 1, 145–147 https://doi.org/10.1007/s41669-017-0028-1

Wheaton, Sarah and Paun, Carmen. (2020, February 14). Europe braces for coronavirus-induced drug shortages with China responsible for most of the EU's pharma ingredients. *Politico*. https://www.politico.eu/article/europe-braces-for-coronavirus-induced-drug-shortages/

Wouters, Olivier & Shadlen, Ken & Salcher-Konrad, Maximilian & Pollard, Andrew & Larson, Heidi & Teerawattananon, Yot & Jit, Mark. (2021). Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. *The Lancet*, 397. https://doi.org/10.1016/S0140-6736(21)00306-8

Wong, G., Tan, L., & Yap, P. (2015). A moral price for medicine. *Singapore medical journal*, *56*(7), 363–365. https://doi.org/10.11622/smedj.2015104

World Health Organization. (2008). Vaccination greatly reduces disease, disability, death and inequity worldwide. *Bulletin of the World Health Organization*, 86 (2), 81-160. https://www.who.int/bulletin/volumes/86/2/07-040089/en/

World Health Organization,Vaccines. (2016). Health Topics. http://www.who.int/topics/vaccines/en/

World Health Organization. (2017). Vaccines Vaccination and trust - How concerns arise and the role of communication in mitigating crises. Accessed on 1sr May 2021 on < https://www.euro.who.int/__data/assets/pdf_file/0004/329647/Vaccines-and-trust.PDF>

World Health Organization. (2017b). V3P: Region Fact Sheet. https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/V3P_Region_Fact_Sheet_EUR.pdf

World Health Organization. (2017c). Fair Pricing Forum - 2017 Meeting Report. https://www.who.int/medicines/access/fair_pricing/FairPricingForum2017MeetingReport.pdf

World Health Organization. (2018). European Vaccine Action Plan 2015-2020 – Midterm report.

World Health Organization. (2018b). Medicines, vaccines and health products. Cancer medicines. Report by the Director-General. EB144/18 144th session 26 November 2018. Available at: http://apps.who.int/gb/ebwha/pdf_files/EB144/B144_18-en.pdf

World Health Organization. (2020). Global Vaccine Market Report. https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1#:~:text=MI4A%20estimates%20global%202019%20market,for%2068%25%20of%20global%20value.

World Health Organization and UNICEF. (2015) Joint Reporting Form for 2013 - Review of vaccine price data. ISBN 978 92 890 5107 1. https://www.euro.who.int/en/publications/abstracts/review-of-vaccine-price-data-submitted-by-who-european-region-member-states-through-the-whounicef-joint-reporting-form-for-2013-2015

World Health Organization. (2020). *Expert Meeting on Market Transparency to Improve Access to High-priced Innovative Medicines*. National Institute For Health And Disability Insurance. https://www.euro.who.int/__data/assets/pdf_file/0008/460943/Access-to-high-priced-innovative-medicines-eng.pdf

World Health Organization, Immunization, Vaccines and Biologicals. (2021). Global Supply. https://www.who.int/immunization/programmes_systems/procurement/market/global_supply/en/