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An Evaluation of Price Determinants and the Economics of Supplying Vaccines:

A Tradeoff Between the Wealth of Firms and the Health of Nations

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Abstract

This paper aims to investigate the price determinants of vaccines, using economic theory and multiple linear regression analysis. Due to uncertain returns of investment in research and development, the volatility of demand, and the winner-take-all element of patent races, supplying vaccines entails substantial risks. To stay in the market, firms need to be compensated for these risks. Expected costs are covered by charging a higher price than the vaccine's marginal cost. Because of risks and high sunk costs, the vaccine industry is predominantly comprised of large firms with market power. The key finding of this paper is that an increase of suppliers of vaccines has a negative effect on vaccine prices. In addition, firms with market power were found to generally charge a higher price. The risk of supply shortages remains a consequence of a high market concentration. These results suggest that competition policy plays an important role in ensuring affordable vaccine provision.

Key words: vaccines, price discrimination, market concentration, patents, risk

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1 Introduction

Affordable vaccines are key to achieve global disease immunity, a part of the Sustainable Development Goals of Agenda 2030 (The United Nations, 2020). Currently, the world is facing a pandemic outbreak of COVID-19, affecting the global population and economy. To protect their population and to minimize the negative effects on the economy, it is in each government's best interest that a vaccine is found and made accessible as early as possible. Due to positive externalities associated with immunization, social optimal price will be at or under the marginal cost (Cook, Jeuland, Maskery, Lauria, Sur, Clemens & Whittington, 2009). However, if vaccines are priced accordingly, rational profit-maximizing firms will not have incentive to go into production (Cook et.al., 2009). To ensure accessibility, a balance should be struck between affordable pricing and adequate firm revenue. In order to serve countries with different willingness to pay while still maximizing profits, firms segment the market into different price groups. With price discrimination, low-income countries are quoted a lower price. Measures of public accessibility further lower the price for low-income countries.

The vaccine market is growing due to technological improvements throughout the pharmaceutical industry (Robbins & Jacobson, 2015). More vaccines are being invented and vaccine schedules are expanding. However, the amount of firms in the vaccine industry has decreased over the past years; previous vaccine manufacturers have allocated their production to the more predictable markets of other pharmaceuticals (Offit, 2005). Several factors contribute to higher risks for firms manufacturing vaccines. While the short term supply is relatively constant, the demand for vaccines is volatile (Michel & Maggi, 2019). The demand for a vaccine depends on circumstances such as prevalence of the disease, which makes firm profit difficult to foresee. Another factor contributing to high risk is the patent landscape. A patent for a vaccine will generate substantial profits for the patentee (Harasimowicz, 2020). However, a patent race is a winner-take-all situation, and remaining firms will not be compensated for research and development investments. As a result of mergers, risks, and high investment costs, the vaccine industry has become highly concentrated (Offit, 2005; Robbins & Jacobson, 2015). High industry concentration is associated with firms being able to use market power to increase price margins (Pepall, Richards & Norman, 2014).

This paper investigates the determinants of vaccine prices by reviewing vaccine market conditions. Several log-linear regressions have been conducted on vaccine price, with explanatory variables measuring the effects of willingness to pay, public accessibility measures, prevalence of price discrimination, and industry concentration. A variable measuring patents could not be included in the regression, but the potential effects are treated on a theoretical basis.

1.1 Purpose and Research Question

Price research of vaccines is necessary in order to create favorable conditions for achieving the United Nations' 2030 impact goals. The purpose of this paper is to provide an overview of the vaccine market. The pricing of the vaccine industry should be understood against the background of the particular market conditions. By assessing price factors and identifying market incentives, this paper provides background for further research and potential policy change. With better understanding of which pricing strategies are used and why, policy-makers can more accurately evaluate the vaccine industry. The question of this research is the following: Which factors determine the price of vaccines?

1.2 Disposition

The following section begins with an explanation of fundamental economic concepts in relation to the vaccine market. The essential features of vaccines as a product are further explained in section 2, along with the key factors affecting vaccine demand. Firm incentives, pricing strategies, and risks associated with production are analyzed in section 4. The section includes subchapters on the patenting landscape and market volatility. Subsequently, section 5 contains an analysis of the vaccine market structure and the effects of market concentration on price. Section 6 contains a presentation of previous research on vaccine price determinants. In the following section 7, the data set used for the regression analysis is presented, along with its limitations. Sections 8 and 9 contain the results and analysis of the regressions. The analysis is followed by a discussion of potential implications for policy in section 10. The conclusion in section 11 contains the paper's main findings and insights, along with suggestions for further research on the topic. In section 12, all references are listed in alphabetical order. Appendices with relevant tests and tables are found in the final section.

2 Background

2.1 The Law of Supply and Demand

The law of supply and demand is a fundamental model for price determination. The relationship is illustrated in a diagram with price on the vertical axis and quantity on the horizontal axis:

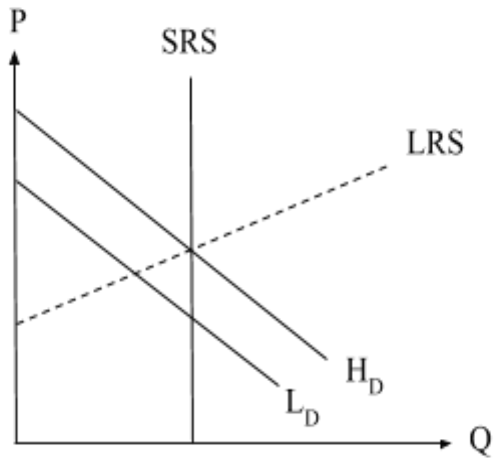

FIGURE 1. The relationship between supply and demand.

where LRS denotes the long-run supply and SRS denotes the short-run supply. H_D signifies a group with high demand, whereas L_D refers to a group with low demand. The market price is found in equilibrium, where the demand and supply curves intersect. When the demand for a product is high, supplying firms are able to charge a higher price. A higher price draws more suppliers to the market, and a lower price attracts more consumers. The quantity is flexible in the long run, but the production of vaccines cannot be immediately adjusted. Thus, the supply is fixed in the short-term. This case is illustrated by the SRS curve being vertical (McGill University, n.d). However, demand can fluctuate quickly, and the prices adjust accordingly (Juvin, 2019).

The price elasticity of demand is illustrated by the slope of the demand curve. Low elasticity of demand represents low responsiveness to price changes, which varies between groups. Inelastic demand can be illustrated as a flat demand curve, and the curve becomes steeper as elasticity increases. The reservation price and elasticity are affected by consumers' preferences for individual products.

Products can be both horizontally and vertically differentiated. Horizontal differentiation refers to different types of the same product, while vertical differentiation involves a difference in quality. For consumers who have preferences for quality, the willingness to pay (WTP) increases for higher quality products (Pepall, Richards & Norman, 2014). Reservation price can also change with the consumer's income. If its income increases, the consumer's demand curve will shift outwards.

2.2 Product Characteristics

A vaccine is a product with certain distinct characteristics. The vaccination of one individual entails a positive externality for others since it minimizes their risk of infection. An externality is an indirect and often unintended cost or benefit for a third party. Since the individual buying a vaccination does not benefit from the full value of the positive externality. Therefore, the amount of people who vaccinate is expected to be lower than socially optimal without state subsidies or other measures are to lower the cost (Cook et.al., 2009). To ensure higher rates of vaccination, vaccines are primarily bought on state-level (WHO, n.d.-a). Vaccination implies both indirect and direct cost benefits: healthy people can stay in the workforce to contribute to a country's economy, and expenditures related to disease (for example hospital care) are avoided (Nichol & Treanor, 2006). The net returns of vaccination depend on the price of the vaccine: the lower the price, the higher the net benefit of vaccination (Cox, Meltzer & Fukuda, 1999).

Furthermore, a vaccine for one disease cannot be substituted for another. As such, vaccines for different diseases are treated as individual markets. Between each vaccine market, demand and price determinants differ. Within the markets, consumers are further categorized into groups based on their WTP for a vaccination.

2.3 Vaccine Demand

The demand of countries essentially depends on the demand of individuals, which is sensitive to several factors. Vaccine demand rises with the prevalence and perceived threat of infection (Pauly, 2000). Optimistic bias is a tendency of individuals believing they have a less-than-average risk of getting infected, which contributes to a cost-benefit miscalculation. The result is increased vulnerability towards disease outbreaks (Darrow, Sinha & Kesselheim, 2018). To illustrate, an outbreak of measles, a highly infectious disease that was thought to be eradicated, occurred in 2014 in the United States. The outbreak is claimed to have been caused by low rates of vaccination, with high infection rates in known anti-vaccination communities (Phadke, Bednarczyk, Salmon & Omerl, 2016). The World Health Organization (WHO) has listed vaccine hesitancy as one of the world's top 10 global health threats (WHO, n.d.-b), further stressing the issue of vaccination refusal.

The individual's propensity to vaccinate is furthermore affected by the perceived risk of vaccination. During the 2009 Swine Flu pandemic, an increased prevalence of narcolepsy was found following the vaccination with Pandemrix. After the outbreak, studies concluded that there was an increased skepticism for mass-vaccination in several countries (Determann, Bekker-Grob, French, Voeten, Richardus, Das & Korfage, 2015; Tulchinsky & Varavikova, 2014). The skepticism resulted in a negative demand shock. An increase of vaccination reluctance shifts the demand curve inwards and results in higher prices. Hence, firm reputation, public information, and media coverage are contributing factors to the price that firms will be able to set. To reassure consumers, certain vaccines have a quality certificate, such as a WHO prequalification. The prequalification is set on certain criteria of safety and efficacy, assessing the manufacturing firms' facilities as well as the vaccine itself (WHO, n.d.-c).[1] Certified vaccine safety is expected to increase demand, as those reluctant to vaccinate may not choose an unqualified product. As prequalified vaccines are of high quality, they are expected to be priced higher than those which are not.

[1] It should be noted that vaccines in general require extensive safety measures to deliver an effective vaccine without the prevalence of serious adverse effects.

3 Market Segmentation

3.1 Income Level

Kondo, Hoshi, and Okubo (2009) estimate a difference in price elasticity of demand for influenza vaccine between elderly people living in urban and rural areas in Japan. The study concludes that those in rural areas have a generally higher price elasticity than those living in urban areas. The result can be explained by rural inhabitants often being of lower income, and therefore being more responsive to price changes (Kondo, Hoshi & Okubo, 2009). With a lower income, there is a higher opportunity cost of paying for vaccines. The propensity to vaccinate and WTP for vaccination is thus closely connected to income elasticity of demand.

A product is categorized as being a normal good if the income elasticity is positive[2], meaning that demand for the product increases with the consumers' income. The result can be applied to countries. Although the value of income elasticity for vaccines is lower than for other healthcare expenditures, it is positive, with low-income countries having a lower income elasticity than high-income countries (Alfonso, Ding & Bishai, 2016).

The higher the income level of a country, the higher its WTP. In the setting of demand and supply, this is illustrated by different income levels having different demand curves. However, because of the constant short-term supply, the demand curves intersect at different price equilibriums. Profit-maximizing firms are expected to charge the highest price possible if the market is large enough. Hence, countries with higher purchasing power will have a higher demanded quantity of vaccines at the market price. Consequently, a lower fraction of the population of poorer countries will be vaccinated in a market with uniform pricing. Therefore, measures by non-governmental organizations have been adopted to increase public accessibility.

[2] The elasticity is measured as an absolute value, and the effect of the elasticity is an increase of demand.

3.2 Public Accessibility Measures

Gavi is an organization that shares vaccine costs with low-income countries (LIC) (Gavi, 2020). With economic aid from Gavi, a larger share of the market for LIC and lower-middle-income countries (LMIC) can be served. The subventions thus result in an upward shift in the demand curve. Another factor contributing to an attainable price for LIC, and some LMIC, is the use of pooled procurement mechanisms (WHO, 2018). Procurement mechanisms refer to the level by which the vaccine was purchased. Pooled procurement entails purchases through organizations such as UNICEF Supply Division and PAHO Revolving Fund, which work to bargain lower prices for LIC and LMIC. With the use of pooled procurement, LIC and LMIC are not quoted the same price as upper-middle-income countries (UMIC) or high-income countries (HIC). The alternative is self-procurement, by which the vaccines are purchased by the country directly. Self-procurement is the mechanism commonly used by UMIC and HIC (WHO, 2018).

3.3 Price Discrimination

When firms charge countries different prices according to their income level and elasticity, they exercise third-degree price discrimination. A price discriminating strategy promotes accessibility of vaccines in LIC, while still allowing price margins when selling to HIC. By doing this, firms can supply markets that would not be served under uniform pricing (Pepall, Richards & Norman, 2014). However, two principal conditions need to be fulfilled to price discriminate. The first is that firms can identify the different groups and their respective WTP. The second condition is that firms can prevent arbitrage, which is sales of products between groups (Pepall, Richards & Norman, 2014). In the vaccine market, the identification problem is easily solved by observing countries' GNI or the use of a procurement mechanism. The arbitrage problem is less easy to solve, due to the difficulty to prevent parallel imports, which is the distribution of goods between downstream parties (Subhan, 2006). It is however solved to the extent that price discrimination is possible.

4 Risks Associated with Vaccine Production

4.1 Market Volatility

The decision to supply a vaccine is based on the expected profit, which is the difference between expected revenue and the expected cost. For investments to be made, the estimated risk-adjusted profit must be positive (Pepall, Richards & Norman, 2014). A feature of the vaccine market is that higher risk entails higher expected revenue, but also higher cost. Hence, if the expected cost is high, the price will be as well. Substantial investment risk is due to the volatile nature of the market. For this reason, profit estimation is particularly difficult. When infection risk decreases, it is reflected in the vaccine market as a negative demand shock. The demand curve shifts inwards, and the equilibrium price is found at a lower level. This was the case when developing a vaccine for the SARS coronavirus. After the development reached the clinical testing phase, the virus essentially disappeared, along with any demand for a vaccine (Roossinck, 2020). Contracts of large quantities are expected to decrease the risk of financial loss, which should lead to lower vaccine prices.

The possibility of increasing production of other pharmaceuticals that require several purchases infers a great opportunity cost to vaccine manufacturers (Robbins & Jacobson, 2015). To maximize the utility of research and development (R&D), firms profit from economies of scope if they can use research for multiple different products. Research of vaccines can to some extent benefit research of other pharmaceuticals. The markets for other pharmaceuticals are less volatile, and entail a safer source of revenue. Because of this alternative cost, a drastic decrease of firms producing vaccines is evident; of the 26 firms with a primary focus on vaccine manufacture in 1967, only five were mainly manufacturing vaccines in 2004 (Offit, 2005).

4.2 Patent Mechanisms

When a firm is successful in developing a vaccine, it will file for a patent and the firm will be granted the sole rights to the intellectual property (IP) during the patent length (Pepall, Richards & Norman, 2014). The Trade-Related Aspects of Intellectual Property Rights

(TRIPS) agreement sets minimum standards for IP rights in the member countries of the World Trade Organization. Least-developed countries are exempt from obligations of TRIPS until 2033, whereas they do not need to protect patent rights (World Trade Organization, 2015). With this agreement, competition is encouraged in least-developed countries. As will be further analyzed in section 5 of this paper, more competition is expected to result in lower prices.

The strength of the patent rights is determined by the breadth and length of the patent. The patent breadth is the scope of the patent. A broad patent implies stronger protection and is often preferred. When the patented IP has a broad scope, it prevents other firms from free-riding on the final product by using the same basic components. However, pharmaceutical patents protect a highly specified formula, for which substitutes need to be clinically tested before patents can be granted (Scherer, F.M, 2000). The patent length is generally 20 years. However, the licensing process can take several years, and the remaining time of IP protection can be few (Mertes & Stötter, 2010). The limited patent length implies that manufacturers must correctly predict that contagion will occur within the 20 years of patent rights. Furthermore, the patentee must annually pay an increasing renewal fee to keep the patent rights (Weiss, 2010). The price of a vaccine is driven up by the expected risk and cost associated with patenting (Darrow, Sinha & Kesselheim, 2018).

Patent regulations are national, whereas a granted patent in one country may be denied in another. It is in the firm's interest to patent its vaccines in as many countries as possible. To reduce costs, the inventor can license the vaccine to governments and private actors for public distribution. The patent acts as a security measure for the patentee, enabling the firm to cover high R&D costs.

Due to legal implications, the timing of a patent affects the expected profit and incentive to produce. If the patent is issued before a health crisis, the patentee obtains full legal rights of the vaccine. However, if the patent is being filed during a health crisis, patent protection is at risk. The TRIPS agreement legitimizes patent infringement under circumstances such as national emergencies (Crouch, 2009). Although the TRIPS states that the patentee is to receive economic compensation after the crisis, this amount is uncertain.

The uncertainty of patent rights decreases the financial incentives to create vaccines during national emergencies when they are ironically needed the most. The TRIPS policy could lead to firms setting higher initial prices to compensate for the weaker strength of their patents. The effect of patents on vaccine price is however difficult to measure. To understand the full impact of patent mechanisms on price, the effect would somehow need to be quantified or further investigated with other methods.

4.3 Patent Racing

A patent implies that only one firm will be compensated for high R&D investments. Therefore, the process of patenting a new formula is often referred to as a patent race (Pepall, Richards & Norman, 2014). Patent racing entails great risk, resulting in high profits for the patentee and high cost for those failing to receive the IP rights. A patent race is illustrated in equation 1. The example is based on the patent race between GlaxoSmithKline (GSK) and Merck & Co. (Merck) for a vaccine for human papillomavirus (HPV). The probability of producing a successful vaccine is denoted as ρ. Further assumptions are that the demand for the vaccine is expressed as $P = A - BQ$, with firms producing at the marginal cost *c*. For simplicity, the set-up costs are ignored in this example.

If both GSK and Merck compete in finding a formula but only one firm is successful, that firm will gain a monopoly position on the HPV vaccine market. If the successful firm is GSK, the expected profit for GSK is:

$$\pi_{GSK} = \frac{(A-c)^2}{4B} \tag{1}$$

while the expected profit for Merck is equal to 0. The probability for this scenario to occur is ρ (1 - ρ). Even if both GSK and Merck are successful with R&D and end up filing a patent, they have a 50 percent probability of obtaining the patent. One firm will be granted the patent, and the other firm will receive 0 profit. The expected profit, occurring with the probability of ρ^2, is:

$$\pi_{GSK} = \pi_{Merck} = \frac{(A-c)^2}{8B}\,. \tag{2}$$

If neither firm success at innovating the vaccine, the profit for each firm is 0. The scenarios illustrate the high risk involved with patent racing, affecting the expected profit. The firms will only invest if the expected profit is high enough (Pepall, Richards & Norman, 2014). There are efficiency losses associated with multiple firms researching the same vaccine without sharing their results. Through cooperation and research joint ventures, firms share cost and profit and thus lower the investment risk. However, cooperation between firms leads to lower profits for each firm after finding and patenting a vaccine. The incentives to enter the market decrease as the number of firms increase. In the outcome of the patent race, Merck and GSK entered a cross-license agreement for HPV vaccines in 2005. Such an agreement allowed both parties to exploit the IP of the patents possessed by the firms. Gardasil was launched in the American market by Merck, and Cervarix was later introduced to the British market by GSK (Amin, Cook-Deegan, Chandrasekharan & Padmanabhan, 2010). Due to patent policies, newer vaccines tend to have a lower amount of manufacturing suppliers, as illustrated by the example of HPV.

5 Vaccine Market Concentration

5.1 Market Structure of the Vaccine Industry

When the patent for a vaccine expires, firms have little incentive to continue their efforts in spreading information about the disease. By acquiring firms with active patents, they can profitably spend resources on marketing the patented vaccines (Richman, Mitchell, Vidal & Schulman, 2017). In addition, an active patent will ensure a safe source of revenue from vaccine sales.

Consequently, market concentration in the vaccine industry has increased since the 1960s due to several mergers and acquisitions (M&As) (Offit, 2005; Robbins & Jacobson, 2015). The four-firm concentration ratio (CR_4) measures the sum of market shares accounted for by the four top firms and is used as a measurement of market concentration (Pepall, Richards & Norman, 2014). In 2017, the CR_4 was estimated to be 90.1%, based on data from a market report (Evaluate Pharma, 2018). As such, the vaccine industry is categorized as being highly concentrated. A recent increase in concentration is shown in table 1.

FIRMS AND MARKET SHARE (%)	2013	2014	2017
GlaxoSmithKline (GSK)	20,9	19,7	24,0
Sanofi Pasteur	21,6	21,9	20,8
Pfizer	15,5	16,8	21,7
Merck & Co	22,6	23,5	23,6
Top four firms	**80,6**	**81,9**	**90,1**

TABLE 1. Market Concentration from 2013 to 2017.[3]

The four top firms in the vaccine industry today, ranked by market share, are GSK, Sanofi Pasteur, Merck, and Pfizer (CNBC, 2020). Well-known vaccines that the firms have developed include HPV vaccine by GSK and Merck, and pneumococcal conjugate

[3] Market shares are measured as the share of worldwide sales (Evaluate Pharma, 2014, 2015, 20)

vaccine(PCV) by GSK and Pfizer. The vaccine market is thus an oligopoly, comprised of a few manufacturing firms with market power.

There are two basic assumptions regarding oligopolies: that firms are rational and that they reason strategically (Pepall, Richards & Norman, 2014). Based on expectations of the behavior of others, a firm will adjust either prices or quantity. Firms in the market are further assumed to act in accordance with profit maximization. In a competitive market, the equilibrium output may be described as:

$$Q^* = \left(\frac{A-c}{B}\right) \cdot \left(\frac{N}{N+1}\right) \tag{3}$$

where N denotes the number of firms in the market, c denotes marginal cost, and Q is the total quantity produced (Pepall, Richards & Norman, 2014). From equation 3, it is evident that more competing firms (larger value of N) lead to a higher industry output. When substituting the expression for the equilibrium output into the equation for the price,[4] it is clear that the price decreases as N increases. Conversely, the equation shows that prices are high when N is low. The actual price margin a firm can set is further determined by the price elasticity of demand. When demand is inelastic, firms can use market power to a higher extent and set higher prices. The relation between elasticity and price margins is illustrated by the Lerner index (LI). The market-wide Lerner index is defined as:

$$LI = \frac{P - \sum_{i=1}^{N} s_i MC_i}{P} = \frac{1}{\eta} \tag{4}$$

where i denotes the index of the observation, s is the market share, P is the price, MC is the marginal cost of the production, and η is a measurement of the elasticity (Pepall, Richards & Norman, 2014). The equation describes the difference in actual price and marginal cost, which reflects the inverse of the price elasticity for the product. When elasticity is low, firms can set higher prices without losing consumers, and vice versa.

[4] The equilibrium price is expressed as P*=A-BQ*

However, market concentration can also lead to lower prices. The vaccine market is characterized by sunk production costs, mainly in the form of investments in R&D. The average cost of each unit sold will hence be higher than the marginal cost. Therefore, there is an economy of scale when producing vaccines that benefit large firms with high production capacity. The marginal cost of R&D can further decrease with the rate of experience of the firm conducting it (Petrova, 2014).

Furthermore, the Schumpeterian hypothesis states that large firms are necessary to ensure innovation when the production entails high fixed costs (Pepall, Richards & Norman, 2014). Should the hypothesis hold for the vaccine industry, it motivates why large firms are an important feature of the market to ensure the development of new vaccines.

5.2 Supply Shortages

With few manufacturers of each vaccine, however, there is a risk of supply shortages. When distribution relies on a limited number of firms, the decrease in output is considerable if one firm fails to produce (Institute of Medicine [US], 2003; Offit, 2005). Supply shortages result in negative supply shocks, shifting the supply curve inwards. Each quantity supplied will consequently have a higher price. Interruptions of supply, higher-than-expected demand and inadequate financing have recurrently caused vaccine shortages (Hinman, Orenstein, Santoli, Rodewald & Cochi, 2010; Offit, 2005). To exemplify, there was an unanticipated shortage of recommended vaccines in the United States at the beginning of 2001. Routine administration of vaccines for eight out of eleven vaccine-preventable childhood infectious diseases was thereby hindered (Institute of Medicine [US], 2003). Furthermore, vaccine shortages lead to higher administration costs, since children who miss vaccinations need to be provided an adequate catch-up schedule (Robbins & Jacobson, 2015). Increased costs are expected to lead to higher prices for the resale of the vaccine. The risk of vaccine shortages due to negative demand shocks is substantial during pandemics (Fedson, 2003). Such a shortage occurred during the 2009 Swine Flu pandemic in the United States (Burns, 2009), disrupting large-scale immunization.

6. Previous Research

6.1 Patents' Effect on Vaccine Prices

In the report "A Fair Shot for Vaccine Affordability" by Médecins Sans Frontières (2017), the effect of patents on vaccine competition and development is examined. Key findings are that patents undermine competition, prevent innovation, and increase uncertainty and prices. According to the study, patents block potential manufacturers from the market. Through firm interviews and patent application analysis, the report identifies anti-competitive behavior in patenting strategies. Generalizing language is used in an attempt to maximize patent breadth. By patenting many components, the patenting for new vaccines including these components require more patent licenses. This strategy is called patent thicketing. Evergreening is another strategy found to be used to prolong monopoly, with firms seeking several patents of the same vaccine. Consequently, increased costs related to vaccine patenting drives up the market price and inhibits global vaccine distribution. The report presents suggestions on how to manage patent barriers to promote vaccine affordability. Countries should apply strict patenting criteria and increase patent filing transparency, and least-developed countries are recommended to use their exemption from the TRIPS agreement to its full extent. Companies are encouraged to increase the price- and IP transparency, refrain from evergreening, and apply affordable licensing terms. Multilateral organizations, such as the WHO, are encouraged to further commit to information sharing, lobby for a global vaccine monitoring mechanism, and support countries' capacity to critically review patents. The report further suggests Gavi to inform more about vaccine patenting and encourage competition by ordering from a variety of suppliers.

6.2 Global Vaccine Market Report

The Market Information For Access (M14A) dataset contains information provided by several countries on behalf of the WHO, and is updated yearly (WHO, 2019a).[5] The data in

[5] The data of the WHO dataset M14A is collected by participating countries, who are responsible for the accuracy of the data reported. The WHO disclaims that it does not guarantee that the information is complete, nor error-free.

M14A has been analyzed by the WHO and presented in their Global Vaccine Market Reports of 2018 and 2019 (WHO, 2018, 2019b). The reports cover vaccine market transparency, volume, and pricing, among other aspects related to the vaccine industry. By running several regressions, the 2018 study finds that self-procurement had a significantly positive effect on price, and HIC paid the highest prices for all but two vaccines (WHO, 2018). A quantity discount of 1.7% was found for every one million doses procured. Given the large amount of doses, this discount was only available to countries with large populations. The study did not observe a significant relationship between increased contract length and price for all income groups, although single-delivery transactions had generally higher prices for middle-income countries. In the more recent M14A report from 2019, some additional results were found. The report concluded that vaccine shortages were a risk. In almost one-third of the 76 vaccine subtypes measured, fewer than four firms were supplying the vaccine for all 182 participating countries (WHO, 2019a). The report also raises concerns about the implications of market segmentation. From 2015 to 2018, there was a 9% increase in price for middle-income countries. The price increase could lead to lower vaccination rates in these countries.

7. Method

7.1 Description and Presentation of the Data Set

In this paper, the determinants of vaccine pricing are investigated with regression analysis, with vaccine price per dose as the dependent variable. In total, the sample of data used contains 3,755 price observations of 21 vaccine types. The data is collected from the M14A dataset, which contains information of 76 vaccine subtypes with a total of 8,450 vaccine observations from 2006-2018. The complete list of variables in M14A is the following: price per dose (in USD), region, income group, Gavi membership, year, vaccine subtype and commercial name, manufacturer, presentation, dosage number, WHO prequalification, procurement mechanism, contract length, the annual number of doses, INCOterm, and VAT percentage. All variables are not included in the regressions conducted in this paper. Variables were chosen based on being potential price determinants, measuring the following areas of interest: market segmentation, risk, and market concentration. A full list of variables used and their presumed effect on price can be found in table 2. To obtain meaningful results, the data used for this paper was further cut based on the following premises:

- observations which did not have information on all variables were excluded to obtain a balanced dataset;
- data on combination vaccines was removed, because of having different product features than single vaccines;
- vaccines with less than 30 observations were removed, based on the presumption that rare diseases have very different price determinants;
- the covered period is reduced to cover 2013-2018 due to a limited amount of observations during 2006-2012;
- VAT (value-added tax) percentage was incorporated into the price to obtain more comparable price information.

In addition to the data from the M14A, the regression contains data of market concentration and firm size as potential determinants of the price. These are two aspects that have been overlooked in previous vaccine price research conducted with regression analysis.

NAME	VARIABLE	TYPE	EXPECTED EFFECT ON PRICE
Comp	Competition	The number of firms producing each vaccine.	Negative effect on price, as firms compete in quality and prices, with lower prices being more competitive.
PQ	WHO Prequalification	A dummy taking the value 1 if the vaccine has been prequalified by the WHO.	Positive effect on price, as consumers have a higher WTP for quality, in accordance to vertical product differentiation.
IG	Income Group	A dummy for each category of income,[6] where LIC is used as a base.	Price is expected to increase with the purchasing power of the consumer, with LIC being quoted the lowest prices, et cetera.
TM	Top Manufacturer	A dummy denoting a top-four manufacturers seen to revenue (Merck, Pfizer, GSK and Sanofi).	Expected positive effect, as high market power enables setting prices above equilibrium.
SP	Self-Procurement	A dummy measuring if the country was procured by one country (0 for pooled).	Positive effect on price, due to third-degree price discrimination and the strong market power of pooled procurement mechanisms.
Q	Total Quantity of Transaction	The contract length of the transaction multiplied with the annual number of doses.	Negative effect on price. This expectation is in accordance with the law of demand and supply.

TABLE 2. Variables used in the regressions.

[6] The countries that reported data are divided up into four income categories. Low-income countries (LIC) have a gross national income (GNI) of $995 or less, lower-middle-income countries (LMIC) have a GNI between $996 and $3,895, upper-middle-income countries (UMIC) have a GNI between $3,896 and $12,055, and high-income countries (HIC) have a GNI of $12,055 or higher.

7.2 Limitations of the Data

The data of the WHO dataset M14A (WHO, 2019a) is collected by participating countries, which are responsible for the accuracy of the data reported (WHO, 2019a). 85% of the WHO member states have reported vaccine purchase data, but there is an unbalance of income group representation, with only 60% HIC reporting data. The number of observations has furthermore increased over time, with a substantial increase in reported orders from 2013 to 2018. Because of having a separate amount of observations for each year, a panel data regression was not possible and years have not been accounted for.

A limitation of the dependent variable concerns the definition of price per dose, which can differ between countries. The WHO emphasizes that some vaccine prices include services such as marketing support and delivery. The price being analyzed is therefore a generalization (WHO, n.d.-d), and potential differences of what it includes have not been taken into consideration. Furthermore, international commerce (INCO) terms have not been taken into account. The INCOterm can account for differences in pricing that are related to which party pays tax on the purchase. It also specifies which risks are associated with the transportation of the goods. The INCOterm does not specify the amount it accounts for, whereas it was excluded in order to simplify the results.

A way to improve the data set would be to incorporate the effect of patents, which most likely affects vaccine pricing. In the absence of a reliable way of measuring and quantifying patent strength and its impact on price, it could not be included as an explanatory variable. The limitations of data should be taken into account when interpreting the results.

7.3 Specification of the Regressions

In this paper, several regressions have been conducted, carried out as multiple regressions using the method of ordinary least squares. Three different levels of significance are provided in the regression tables (0.01, 0.05, and 0.1), with p-values lower than 0.01 denoting the most significant variables. A confidence interval of 95% has been used to decide whether or not the explanatory variables have a significant effect on the dependent variable.

When its p-value is lower than 0.05, the explanatory variable is interpreted as having a significant effect. The R-squared value explains how much of the variance can be explained.

Tests for heteroscedasticity, multicollinearity, and misspecification have been conducted. There was a presence of heteroscedasticity, which was accounted for by including robust standard errors. To test for multicollinearity, a variance inflation factor (VIF) test was run. The result showed a low correlation between the variables, and multicollinearity was ruled out as a problem in both regressions. A presentation of the full range of tests can be found in appendix A of this paper. The Ramsey RESET test showed signs of misspecification, whereas a regression with a logged dependent variable with base 10 and untransformed explanatory variables had the best fit. Still, the Ramsey reset test indicates signs of misspecification. However, explanatory variables were not non-linearly transformed, to give the results a more clear interpretation. Table 3 contains information on how to interpret the notation used in the regression specification.

The interpretation of a log-linear model is not straightforward. To understand the direct effects of explanatory variables on price, certain calculations have been made. The direct is found by multiplying the price by 10 raised to the power of the unit change with the regression coefficient. For dummy variables, the unit change is 1. The quantity variable has been scaled by 100,000 since a one-unit increase of vaccine dose is negligible. As their unit change is can be larger than 1, competition and quantity coefficients are adjusted by raising 10 to the product of the regression coefficient and the new unit change. Coefficients derived from the formula explained above can be found in column P in table 5.[7] The variables' effect on price is calculated by multiplying the price by these new coefficients shown.

NOTATION	INTERPRETATION
$logP_i$	The logarithm of the price variable
β_1	Constant of the regression
β_i	Coefficient of the variable *i*

TABLE 3. Notations used in the specification of regressions.

[7] Table 6 including column P is presented in appendix B, named Table 6B.

Regression 1 has been conducted with the intent of explaining the price determinants of the vaccine market on a general level. By running one regression on all vaccines, the aim is to identify the overall impact and direction of the price determinants. The specification of regression 1 is the following:

$$log\ P_i = \beta_1 + \beta_2 Q + \beta_3\ Comp + \beta_4\ PQ + \beta_5\ SP + \beta_6\ LIC + \beta_7\ LMIC + \beta_8\ UMIC + \beta_9\ HIC + \beta_{10}\ TM + \varepsilon_i \tag{1}$$

A limitation of regression 1 is that it does not consider the difference of determinants between vaccines. As explained, vaccines have varying demands and are to be treated as separate markets. To obtain insights into how price determinants can differ, regressions were conducted on separate vaccine types. The objective of this paper is to investigate price determinants, but also which factors affect the incentives of manufacturing firms. When investigating the vaccines generating the highest revenue, it was found that the top four vaccines account for 82,75% of the total market revenue. These are presented in table 5, which shows the respective quantity, mean price, total revenue in millions of dollars, and competition. A full list of the vaccines and their respective revenue can be found in appendix B in section 13.

VACCINE	QUANTITY	MEAN PRICE	REVENUE	COMP.	TOTAL OBS.
PCV	1 504 098 590	$4,4	$ 6,640M	3	376
HPV	119 428 050	$24,7	$ 2,940M	2	186
Seasonal Influenza	824 789 746	$2,5	$ 2,030M	17	107
Rota	753 220 702	$2,6	$ 1,970M	14	205
Varicella	59 712 463	$19,8	$ 1,180M	20	52

TABLE 4. Information on the five vaccines generating the most revenue.

The most sold vaccine is PCV, which is sold at a relatively low price compared to the other vaccines generating the highest revenue. The most expensive vaccine is HPV, with the second to least quantities sold of the presented vaccines. Both PCV and HPV are essentially produced by two only manufacturers.[8] Vaccines for rotavirus and seasonal influenza have similar prices and quantities sold, with seasonal influenza having slightly more quantities sold at a somewhat lower price. Both these vaccines were produced by relatively many manufacturers. Varicella has the lowest quantity sold and is the second most expensive vaccine of the five listed. For this vaccine, there were 20 manufacturing firms, which is high relative to that of the other vaccines. As the five vaccines in table 4 account for a predominant part of the industry revenue, they are a good representation of markets that firms have incentives to enter. Therefore, their price determinants are of particular interest in this paper. Regressions on the five vaccines have thus been conducted and can be found in table 5. The specification of the regressions is as follows:

$$log\, P_i = \beta_1 + \beta_2 Q + \beta_3\, PQ + \beta_4\, SP + \beta_5\, LIC + \beta_6\, LMIC + \beta_7 UMIC + \beta_8\, HIC + \varepsilon_i \quad . \tag{2}$$

Regression 2 contains all variables included in regression 1 apart from TM and Comp. These variables were omitted from this regression due to a lack of variance in the observations.

[8] The third manufacturer of PCV accounted for only one order.

8. Results

Table 5 contains the results of regression 1. Table 6 presents the results of regression 2, conducted on the five vaccines generating the highest revenue.

VARIABLES (1)	*log P*	*P*
Q	-4.40e-09***	0.999
	(7.24e-10)	
Comp	-0.0652***	0.861
	(0.00160)	
PQ	-0.225***	0.596
	(0.0197)	
SP	0.356***	2.270
	(0.0221)	
LMIC	0.0828***	1.210
	(0.0186)	
UMIC	0.343***	2.203
	(0.0224)	
HIC	0.685***	4.842
	(0.0274)	
TM	0.393***	2.472
	(0.0201)	
Constant	0.411***	2.576
	(0.0348)	
Observations	3,755	
R-squared	0.741	

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

TABLE 5. Regression 1 conducted on all vaccine types simultaneously.

All variables of regression 1 showed highly significant effects on price. Quantity, competition, and WHO prequalification have a significantly negative effect on price. Self-procurement, top manufacturer, and all countries in a higher income group than LIC have a positive effect on price. The regression showed clear evidence of market segmentation. Self-procurement has a significantly positive effect on price, with self-procuring countries paying more than double the price of others. All income group variables have significant effects on price. With LIC as the baseline, the regression revealed that the mean price of a vaccine is generally 1.2 times higher for LMIC and 2.2 times higher for UMIC. The price difference between LIC and HIC was the highest. Market concentration was found to have a negative effect on price. Top four manufacturers generally set prices higher than other manufacturers. Increased quantity of transaction was found to lower the price but by a minuscule amount of 1% per every 100,000 doses. Contrary to initial expectations, WHO prequalification resulted in lower prices.

VACCINES	PCV	HPV	Seasonal Influenza	Rota	Varicella
VARIABLES (2)	*logP*	*logP*	*logP*	*logP*	*logP*
Q	-2.21e-09***	-2.42e-08*	-3.12e-09	-4.53e-09***	-7.51e-09
	(8.14e-10)	(1.27e-08)	(1.98e-09)	(1.45e-09)	(9.48e-09)
PQ	0.0799***	-0.369***	0.0845**	0.535***	0.0126
	(0.0272)	(0.0796)	(0.0415)	(0.0705)	(0.0512)
SP	0.416***	0.375***	0.148***	0.193***	0.233***
	(0.0363)	(0.0516)	(0.0336)	(0.0587)	(0.0335)
LMIC	0.0739***	0.0266		-0.00147	
	(0.0208)	(0.0378)		(0.0255)	
UMIC	0.427***	0.234***	0.00901	0.316***	
	(0.0401)	(0.0363)	(0.0491)	(0.0452)	
HIC	0.671***	0.501***	0.205***	0.771***	0.111**
	(0.0412)	(0.0636)	(0.0521)	(0.0704)	(0.0426)
Constant	0.451***	1.065***	0.349***	-0.132*	1.120***
	(0.0312)	(0.0828)	(0.0465)	(0.0749)	(0.0249)
Observations	377	186	272	211	75
R-squared	0.846	0.708	0.304	0.748	0.342

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1

TABLE 6. Regression 2 conducted on the five vaccines generating the most revenue.

Table 6 contains five regressions conducted on separate vaccines. Quantity has a highly significant negative effect on prices of PCV and rota vaccines. Quantity has no significant effect on the prices of vaccines for seasonal influenza or varicella. WHO prequalification has a highly significant effect on the prices of all measured vaccines apart from varicella. The effect was positive on PCV and seasonal influenza, but negative for HPV. All income groups have a significantly positive effect on the prices of PCV. Due to a lack of observations of purchases from LIC, the LMIC variable was omitted from the regressions conducted on vaccines for seasonal influenza and varicella to replace the missing baseline. For the same reason, UMIC was omitted from the regression on the varicella vaccine. Furthermore, LMIC was not significant for HPV.

9 Analysis

The focus of this analysis is to interpret how the result of regression 1 relates to market segmentation, risk-reducing measures, and market concentration. In most cases, the results of regression 2 confirm the result of regression 1. However, the price determinants differ between vaccine types. The difference is exemplified by a few noteworthy exceptions of the five vaccines generating the highest revenue.

The observed price difference between income groups confirms the result of the previous WHO studies, which concluded that there is a high prevalence of price discrimination (WHO 2018, 2019a). In accordance with theory, the general regression showed that higher income groups pay more than lower income groups for the same vaccine. This strategy aligns with profit maximization for vaccine manufacturers since the consumer group is broadened by market segmentation.

Third-degree price discrimination is facilitated by lower income groups often using pooled procurement mechanisms. By providing a discounted price for groups using pooled procurement, firms solve the identification problem of price discrimination. Confirming initial expectations, self-procurement has a positive effect on price in both the general regression and the regression run on separate vaccines. The pooled procurement mechanism is mainly used by LIC, which are predominantly members of Gavi. As previously stated, this group is generally quoted a lower price. Another reason for the price differences can be the bargaining power of the organizations negotiating. By purchasing large quantities of vaccines from a variety of firms, UNICEF Supply Division and PAHO act as both procurement mechanisms and competition controllers.

The consumers' WTP for a vaccine partly depends on the perceived risk of the vaccination. In this paper, the variable used for measuring risks associated with vaccination is WHO prequalification. The prequalification is set for vaccines of high quality and indicates vertical product differentiation. According to theory, higher quality implies a higher WTP, and a possibility for firms to set higher prices. However, regression 1 showed that a WHO prequalification generally has a negative effect on vaccine prices. This result can be explained by prequalified vaccines having higher demand. With a larger market, manufacturers can lower prices if the production involves economies of scale. A majority of orders during the measured period were of prequalified vaccines, supporting this claim. The firms' incentives to obtain a prequalification increase due to its higher demand. Hence, it is a risk-reducing feature for both consumers and manufacturers. Conclusively, higher quality has a negative effect on price and presumably positive effect on demanded quantity. For the 21 vaccines included in regression 1, the effect of demand is generally larger than the effect of quality. However, for a majority of the five measured vaccines, prequalification has a positive effect on price. This result confirms initial expectations of the variable; consumers have a higher WTP for prequalified vaccines, allowing for firms to set higher price-margins. On the price of varicella, WHO prequalification did not have a significant effect. The non-significance could partly be explained by the amount of prequalified varicella vaccines being relatively low. A conclusion of the effect of this variable is thus difficult to draw.

Risk-reducing features lead to higher risk-adjusted returns for firms. Contracts of large quantities function as a way of hedging towards demand fluctuations, as it guarantees the supply to be sold. With higher risk-adjusted returns, the firms are able to sell at a lower price while generating the same expected profit. Total transaction quantity has a significant effect on price, showing signs of firms offering a quantity discount. The result suggests that a method for obtaining cost efficiencies is to purchase a large quantity of vaccine doses. All the four vaccines responsible for most revenue had a significantly lower price associated with a larger quantity of total transaction, besides those for varicella and seasonal influenza. Varicella is the vaccine (of the five further investigated) that accounted for the lowest amount of doses sold. For seasonal influenza, there is a new version of the vaccine every season. The insignificant effect of quantity can be explained by the production not reaching the volumes needed to lower costs with economies of scale.

With more manufacturers of a vaccine, price competition leads to lower prices, confirming expectations based on the theory presented in section 5 of this paper. When products are considered perfect substitutes, the firm setting the lowest price will serve the whole market. As vaccines for the same disease are substitutable to a high extent, firms are expected to set similar prices as to not lose consumers to competitors. The variable measuring the effect of a top-four manufacturer shows that firms with market power indeed set higher prices. As illustrated by the Lerner index in section 5, this result is to be expected based on the presumption of low price elasticity of demand for vaccines. The top four firms are further expected to set higher prices due to consumers having a higher WTP for products manufactured by firms with high legitimacy.

PCV and HPV are the two vaccines generating the highest revenue. Both are predominantly produced by only two manufacturers, both of which being a top-four firm. The prices are thus partly determined by the market being an oligopoly; the prices between the firms depend on those of their competitors. The effect on price differed between the vaccines. While PCV vaccines have relatively low prices, those for HPV are high. For PCV vaccines, the firms Pfizer and GSK have a mean price similar to each other, only differing $1.14. The small difference in price is expected because of firms engaging in price competition. According to oligopolistic theory, Pfizer, with the lower price, will gain most consumers if the vaccines are considered close substitutes. Confirmatively, Pfizer is responsible for a higher amount of sales. As for HPV vaccines, Gardasil by Merck is priced $12.52 higher than Cervarix by GSK. If the Gardasil and Cervarix would be considered perfect substitutes, Merck would need to lower their price not to lose all consumers to GSK. However, demand for the vaccines can differ due to horizontal differentiation, motivating that Merck can profitably charge the higher price for Gardasil.

10 Discussion: Possible Implications for Policy

This paper has thus far investigated how market segmentation, risks associated with production, and market concentration affect the pricing of vaccines. Price determinants have been investigated on both a general level and on a specific level for five vaccines. This section contains a discussion on how these insights can affect policy in order to achieve the immunization goals of Agenda 2030.

Price discrimination is necessary for affordability. Without quoting LIC lower prices, this market might not have been served by profit-maximizing firms. However, as prices decrease for countries of lower income, countries of higher income need to pay more. This results in possible concerns for vaccine accessibility, as prices of middle-income countries have increased during the past years (WHO, 2019b). As shown in section 3, the income elasticity for vaccines is relatively small (Alfonso, 2016). When income for LIC increases, they are no longer eligible for Gavi support. The propensity to vaccinate might thus stagnate or decrease, despite an advance in income level. This result calls for more economic aid to LMIC that are no longer Gavi eligible.

Both pooled procurement and price discrimination lower prices for LIC and LMIC. Consequently, they discourage production for the market of lower-income countries. There are diseases affecting LIC which do not yet have vaccines developed for them. A possible explanation is that the diseases mainly target LIC, from which firms cannot quote a high price. Profitability and incentives to enter these markets need to be higher. Again, these aspects need to be kept in mind when formulating policy and call for organizations (such as Gavi) to share costs rather than negotiating lower vaccine prices.

A WHO prequalification is a risk-reducing measure for both consumers and firms. The legitimacy of the prequalification relies on the WHO as an effective quality assessor, whereas their continuous work is important. However, the WHO may take further actions to increase demand and lower the expected costs of firms. Measures to prevent the rise of anti-vaccination movements create a larger market for vaccines. More firms could then be profitable in production and increase price competition. One way to accomplish this is by requiring that more vaccines are quality assessed when entering the market.

Production risks can be reduced by altering patent policy. By shortening the length of patents, entry barriers for new manufacturers are lowered. However, a shorter length implies more pressure on the patent proprietor to cover costs, probably marking up the price during the patent length. Regulating vaccine prices with patent policy is a short-term tradeoff between affordability and secured vaccine supply. With a less rigid patent policy, more cost-saving innovations can be made by smaller firms that do not have the means to develop a new vaccine formula. However, a decrease in the expected profit for the firm winning the patent race leads to smaller incentives for innovation.

The process of patenting can further explain the price differences between HPV and PCV. The two firms developing HPV vaccines entered a cross-licensing agreement, while the firms producing PCV did not. Manufacturers of PCV are required to set strategic prices that take the competitors price into consideration. Because of the two different HPV vaccines launching in different markets, the firm responsible for each market obtained monopoly power in that territory. With no competitors, firms can set high price margins. A cross-licensing agreement thus results in higher prices. However, such an agreement can be justified by creating larger incentives for producing the vaccine. Shared cost entails less risk, and firms are thus more likely to obtain positive risk-adjusted returns on the investment. The inefficiency of independent research implies the need for mechanisms promoting R&D collaboration.

Incentives determine how many firms will be active in the market, and thus affect the market concentration. Economic theory suggests that market concentration has two main effects on prices. Prices can fall if large firms have cost advantages in production, but can also rise if they exploit their market power. In the regression presented in this paper, the latter effect was found to be stronger. That firms with market power set high price margins implies a tradeoff between incentives for vaccine development and vaccine affordability. When formulating policy, this tradeoff needs to be kept in mind. A low number of suppliers can be explained by high R&D costs, as stated in the Schumpeterian hypothesis. The example of two large firms producing both HPV and PCV is insufficient in order to adopt the Schumpeterian hypothesis, but it does indicate its relevance. Other measures than a more regulated competition policy should be favored for this reason. To reduce market concentration, firms could be offered a premium or tax reductions for producing vaccines instead of other drugs. A possible result of this measure is that more firms can be profitable in vaccine production.

11 Conclusion

Price discrimination enables more people to vaccinate. Wide-spread immunization is dependent on affordability and innovation: low prices enable more people to vaccinate, but high prices give more incentives for firms to develop vaccines. With the world facing the COVID-19 pandemic, the need for accessible vaccines has become ever so urgent.

Research on vaccine accessibility is required in order to prepare for future health crises. The purpose of this paper was to provide a comprehensive background to vaccine pricing, which is the result of a complex market with several conflicts of interest. Understanding vaccine price determinants is vital to assess the prospect of assuring global health and publically accessible vaccine supply.

In this paper, vaccine prices have been found to increase with market concentration, market power, and GNI. Pooled procurement mechanisms lead to lower prices because of effective price negotiations. Third-degree price discrimination based on income was found to be prevalent. Furthermore, a WHO prequalification generally lowered the price for vaccines, with some exceptions. By quantifying the effects of competition and top manufacturers, this research has provided important insight on the role of market power on vaccine prices.

The vaccine prices quoted to middle-income countries have increased during 2013-2015. The increase raises accessibility concerns, as the income elasticity of vaccination is generally low. Further research should be conducted on especially lower-middle-income countries' propensity to vaccinate after having risen in income level. With such research, policy suggestions can be made to ensure accessibility to this group.

The current patent policy has two main effects on vaccine accessibility. On the one hand, patents protect the profits of the innovator of the formula and thus creates incentive for firms to invest in expensive R&D. On the other hand, the current patent policy serves as an entry barrier and limits the competition between firms in the market, potentially resulting in high prices for consumers and lower accessibility of the vaccine. The latter effect was shown to be especially strong in the market for HPV vaccines. Further research investigating the strength of patents is needed, in order to interpret its effect on price with more accuracy. With more research, policy reforms that further lower entry barriers could be suggested.

Besides leading to higher prices, having few manufacturers of vaccines leaves the market vulnerable. Should one manufacturer experience an unexpected shortage, the remaining firms might not be able to support the whole production. However, when drawing a conclusion on how to use this information when reviewing competition policy, the structure of the market should be taken into consideration. As the Schumpeterian hypothesis suggests, the vaccine market could suffer in terms of innovation without large firms that have the capacity to afford high investment costs. If firms are dependent on scale economies to be successful, this condition can explain and justify the high market concentration. To further investigate the relevance Schumpeterian hypothesis, research could be conducted of which firm size accounts for the highest amount of vaccine innovation.

The vaccine market is growing, with improved technology leading to more frequent discoveries of vaccines for both new and old diseases, providing opportunities for firms to earn profit. Ensuring the accessibility of vaccines relies on affordable vaccines being offered, but also on firms having sufficient incentives to supply the market. Many of the measures to increase accessibility discussed in this paper can possibly have the unintended effect of leading to a lower number of supplying firms. Global vaccine accessibility and affordability requires a balance of low consumer prices and profit incentives for manufacturing firms. To reach the goals of Agenda 2030, policymakers, including competition authorities, should take the mentioned tradeoffs into consideration.

12 References

Alfonso, N, Ding, G, Bishai D. (2016). Income Elasticity of Vaccines Spending Versus General Healthcare Spending, *Health Econ*, vol. 25, no. 7, pp. 860-72, Available online: https://doi.org/10.1002/hec.3190 [Accessed 20 May 2020]

Amin, T., Chandrasekharan, S., Cook-Deegan, R., Padmanabhan, S. and Sampat, B. (2010). Intellectual Property, Technology Transfer and Manufacture of Low-cost HPV Vaccines in India, *Nat Biotechnol* vol. 28, no.7, pp. 671–678. Available online: https://doi.org/10.1038/nbt0710-671[Accessed 3 May 2020]

Burns, J. (2009). Health Officials Frustrated by the H1N1 Shortage, The Wall Street Journal, 4 Nov, Available online: https://www.wsj.com/articles/SB125735930128328447 [Accessed: 8 April 2020

CNBC. 2020. Coronavirus highlights the $35 billion vaccine market. Here are the key players, Available at: https://www.cnbc.com/2020/02/21/coronavirus-brings-light-to-the-35-billion-vaccine-market.html [Accessed 15 April 2020]

Crouch, D. (2009). Nil: The Value of Patents in a Major Crisis such as an Influenza Pandemic, *Seton Hall Law Review,* vol. 39, no. 1125, Available at: https://scholarship.law.missouri.edu/cgi/viewcontent.cgi?article=1430&context=facpubs [Accessed 10 April 2020]

Cook, J, Jeuland, M, Maskery, B, Lauria, D, Sur, D, Clemens, J, Whittington, D. (2009) Using Private Demand Studies to Calculate Socially Optimal Vaccine Subsidies in Developing Countries, *J Policy Anal Manage*, vol. 28, no. 1, pp. 6–28 Available online: https://efdinitiative.org/sites/default/files/cook20et20al20200820jpam20herd.pdf [Accessed 22 April 2020]

Cox, J., Meltzer, I.M., Fukuda, K. (1999). The Economic Impact of Pandemic Influenza in the United States: Priorities for Intervention, *Emerging Infectious Diseases Journal*, vol. 5, no. 5, pp. 659-671, Available online: https://pubmed.ncbi.nlm.nih.gov/10511522/ [Accessed 22 April 2020]

Darrow, J., Sinha, M. & Kesselheim, A. (2018). When Markets Fail: Patents and Infectious Disease Products, *Food and Drug Law Journal,* vol. 3, no. 73, pp. 361-382, Available online: https://www.jstor.org/stable/e26661182 [Accessed: 21 April 2020]

Determann, D, Bekker-Grob, E, French, J, Voeten, H, Richardus, J, Das, E, Korfage, I. (2015). Future Pandemics and Vaccination: Public Opinion and Attitudes Across Three European Countries, *Vaccine*, vol. 34, no.16, pp. 802-8, Available online: https://doi.org/10.1016/j.vaccine.2015.12.035 [Accessed 10 May 2020]

Evaluate Pharma. (2014). World Outlook Preview 2014, outlook to 2020, Evaluate Pharma, Available online: https://info.evaluategroup.com/rs/evaluatepharmaltd/images/EP240614.pdf [Accessed 5 May 2020]

Evaluate Pharma. (2015). World Outlook Preview 2015, outlook to 2020, Evaluate Pharma, Available online: https://info.evaluategroup.com/rs/607-YGS-364/images/wp15.pdf [Accessed 5 May 2020]

Evaluate Pharma. (2018). World Outlook Preview 2018, outlook to 2024, Evaluate Pharma, Available online: https://www.evaluate.com/thought-leadership/pharma/evaluatepharma-world-preview-2018-outlook-2024 [Accessed 5 May 2020]

Fedson, D. (2003). Pandemic Influenza and the Global Vaccine Supply, *Clinical Infectious Diseases*, vol.36, no. 12, pp. 1552-1556, Available online: https://doi.org/10.1086/375056 [Accessed 17 May 2020]

Gavi. (2020). About, Available online: https://www.gavi.org/our-alliance/about [Accessed 5 April 2020.]

Harasimowicz, R. (2020). The Global Patent Race for a COVID-19 Vaccine, *The National Law Review*, 24 March, Available online: https://www.natlawreview.com/article/global-patent-race-covid-19-vaccine [Accessed: 5 April 2020]

Hinman, A, Orenstein, W, Santoli, J, Rodewald, L, Cochi, S. (2006). Vaccine Shortages: History, Impact and Prospects of the Future, *Annu. Rev. Public Health 2006,* no. 27, pp. 235-59, Available online: https://www.annualreviews.org/doi/pdf/10.1146/annurev.publhealth.27.021405.102248 [Accessed 4 April 2020]

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, 5th ed. Washington DC: National Academies Press (US), Available online: https://www.ncbi.nlm.nih.gov/books/NBK221813/ [Accessed 16 May 2020]

Kondo, M., Hoshi S., and Okubo, I. (2009). Does Subsidy Work? Price Elasticity of Demand for Influenza Vaccination Among the Elderly in Japan, *Health Policy,* vol. 91, no. 3, pp. 269-276, Available online: https://doi.org/10.1016/j.healthpol.2008.12.014 [Accessed 20 April 2020]

McGill University. (n.d). Supply and Demand, McGill University, Available online: https://www.cs.mcgill.ca/~rwest/wikispeedia/wpcd/wp/s/Supply_and_demand.htm. [Accessed: 10 April 2020]

Médecins Sans Frontières. (2017). A Fair Shot for Vaccine Affordability: Understanding and addressing the effects of patents on access to newer vaccines, Médicines Sans Frontières, Available at: https://www.msfaccess.org/sites/default/files/VAC_report_A Fair Shot for Vaccine Affordability_ENG_2017.pdf (Accessed: 28 April 2020)

Juvin, P. (2019). Complexity of Vaccine Manufacture and Supply, in Michel, J & Maggi, S. (eds), *Adult Vaccinations: Changing the Immunization Paradigm*, Cham: Springer, pp.1-5

Nichol, K. L. & Treanor, J. T. (2006). Vaccines for Seasonal and Pandemic Influenza, *The Journal of Infectious Diseases,* vol. 194, suppl. 2. pp. S111-8, Available online: https://academic.oup.com/jid/article/194/Supplement_2/S111/850453

Olive, J., Hotez, P., Damania, A and Nolan, M. (2018). The State of the Anti Vaccine Movement in the United States: A Focused Examination of Nonmedical Exemptions in states and counties, *PLOS Medicine,* vol. 15, no.7, n.p., Available online: https://doi.org/10.1371/journal.pmed.1002578 [Accessed 23 April 2020]

Pepall, L., Richards, D. & Norman, G. (2014). Industrial Organization: contemporary theory and empirical applications, 5th edn, New Jersey: Wiley

Petrova, E. (2014). Innovation in the Pharmaceutical Industry: The Process of Drug Discovery and Development, in Ding, M., Eliashberg, J., Stremerch, S. (eds), *Innovation and Marketing in the Pharmaceutical Industry*, New York: Springer, pp. 19-83, Available online: https://link.springer.com/content/pdf/10.1007%2F978-1-4614-7801-0.pdf [Accessed 17 May]

Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. (2016). Association Between Vaccine Refusal and Vaccine-Preventable Diseases in the United States: a Review of Measles and Pertussis, *JAMA*, 2016; vol. 315, no. 11, pp. 1149-1158, Available online: https://www.ncbi.nlm.nih.gov/pubmed/26978210 [Accessed 10 April 2020]

Richman, B., Mitchell, W., Vidal, E. & Schulman, K. (2017). Pharmaceutical M&A Activity: Effects on Prices, Innovation, and Competition, *Loyola University Chicago Law Journal*, vol. 48, pp.787-819, Available online: https://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=6441&context=faculty_scholarship

Robbins, M & Jacobson, S. (2015). Analytics for Vaccine Economics and Pricing: Insights and Observations, *Expert Review of Vaccines*, vol. 14, no. 4, pp. 605-616, Available online: https://pubmed.ncbi.nlm.nih.gov/25435003/ [Accessed 13 May 2020]

Roossinck, M. (2020). Scientists were close to a coronavirus vaccine years ago. Then the money dried up, The Conversation, May 5, Available online: https://theconversation.com/the-mysterious-disappearance-of-the-first-sars-virus-and-why-we-need-a-vaccine-for-the-current-one-but-didnt-for-the-other-137583 [Accessed 10 April 2020]

Offit, P. (2005). Why Are Pharmaceutical Companies Gradually Abandoning Vaccines? Health Affairs, vol. 24, no.3, pp. 623-630, Available online: https://pubmed.ncbi.nlm.nih.gov/15886152/ [Accessed 10 May 2020]

Scherer, FM. (2000). The Pharmaceutical Industry, in Culyer, A.J & J.P Newhouse (eds), *Handbook of Health Economics*, Amsterdam: Elsevier, pp.1927-1336

Subhan, J. (2006). Scrutinized: The TRIPS Agreement and Public Health, McGill Journal of Medicine, vol. 9, no. 2, pp. 152-159, Available online: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323529/ [Accessed 8 May 2020]

The United Nations. (2020). Sustainable Development Goal 3, Available online: https://sustainabledevelopment.un.org/sdg3 [Accessed 21 April]

Tulchinsky, T. & Varavikova E. (2014). The New Public Health, 3rd edn. Academic Press: San Diego

Weiss, Pia. (2010). Patent Policy: Legal-Economic Effects in a National and International Framework, New York: Roxon

White, Corey (2016). Measuring the Social and Externality Benefits of Influenza Vaccination, job market paper, University of California, Santa Barbara, Available online: https://static1.squarespace.com/static/5537e3fbe4b0be6b2048ea5f/t/5d13e63be3ab90000173bd29/1561585221199/Revision_White_Flu_June2019.pdf [Accessed 18 May 2020]

WHO. (n.d.-a).Vaccine Market. Available online: https://www.who.int/immunization/programmes_systems/procurement/market/global_demand/en/ [Accessed: 10 April 2020]

WHO. (n.d.-b). Ten threats to global health in 2019. Available online: https://www.who.int/news-room/feature-stories/ten-threats-to-global-health-in-2019. [Accessed 5 May 2020]

WHO. (n.d.-c). About WHO prequalification of vaccines. Available online: https://www.who.int/medicines/regulation/prequalification/prequal-vaccines/about/en/ [Accessed: 14 April 2020]

WHO. (n.d.-d). Factors to consider when comparing vaccine prices, WHO, Available online: https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/factors_to_consider.pdf?ua=1 [Accessed: 29 April 2020]

WHO. (2018). Global Vaccine Market Report, WHO, Available online: https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/MI4A_Global_Vaccine_Market_Report.pdf [Accessed: 10 April 2020]

WHO. (2019a). MI4A: Vaccine Purchase Data, Available online: https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module1/en/. [Accessed: 8 April 2020]

WHO. (2019b). Global Vaccine Market Report, WHO, Available online: https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2019_Global_Vaccine_Market_Report.pdf?ua=1. [Accessed: 10 April 2020]

World Trade Organization. (2015). WTO members agree to extend drug patent exemption for poorest members, Available online: https://www.wto.org/english/news_e/news15_e/trip_06nov15_e.htm [Accessed: 10 April 202

Appendix A: Tests

VARIABLE	VIF	1/VIF
Q	1.04	0.957965
Comp	1.51	0.661615
PQ	1.30	0.769649
SP	1.80	0.554339
LMIC	2.07	0.484250
UMIC	2.67	0.374231
HIC	3.67	0.272561
TM	1.64	0.609149
Mean VIF	1.96	-

TEST 1. Variance inflation factor (VIF) Test on regression 1.

A variance inflation factor (VIF) test was used to test for multicollinearity. VIF is calculated as $\frac{1}{1-R^2}$. The numerical value is the percent of standard error inflated in the coefficient. 1 signifies that there is no correlation, whereas there is a moderate correlation up to 5. A value above 5 implies a high correlation. At most, HIC demonstrates a moderate correlation at 3.57. Therefore, we disregard suspicion of multicollinearity as a problem in the regression

Ho: model has no omitted variables

F(3, 3743) = 39.23

Prob > F = 0.0000

TEST 3. Ramsey RESET test using powers of the fitted values of log P (regression 1)

Ramsey Reset test is a test for misspecification. The test result indicates that there is a non-linear model that is better fit for the regression.

Ho: Constant variance
Variables: fitted values of Log_P
chi2(1) = 5.58
Prob > chi2 = 0.0181

TEST 5. Breusch-Pagan / Cook-Weisberg test for heteroskedasticity of regression 1

The presence of heteroscedasticity was taken into account by using robust standard errors when running the regression.

Appendix B: Tables

VACCINE	% OF TOTAL	VACCINE	% OF TOTAL
BCG	11,60%	PPSV	2,30%
bOPV	11,00%	Rabies	2,80%
HepA	4,40%	Rota	6,30%
HepB	15.0%	Seasonal Influenza	8,10%
Hib	2,80%	TBE	0,90%
HPV	5,50%	tOPV	1,60%
IPV	9,20%	TT	4,20%
JE	1,10%	Typhoid Ps	1,10%
Measles	4,20%	Varicella	2,20%
MenC conj.	1,00%	YF	5,10%
PCV	11,20%	TOTAL	100%

TABLE 1B. Order frequency of vaccines included in regression 1.

Competition	% of total	Competition	% of total
2	6.98	8	13.40
3	10.04	9	3.91
4	6.44	11	2.50
5	7.99	14	13.69
6	2.00	16	10.39
7	1.97	17	20.69

TABLE 2B. Frequency of amount of competition.

VARIABLE	Frequency (%)
LIC	14,7%
LMIC	24,2%
UMIC	29,6%
HIC	31,3%
Self Procurement	49,8%
WHO Prequalification	69,8%

TABLE 3B. Frequency of variables.

VACCINE	QUANTITY	MEAN PRICE	REVENUE	TOTAL OBS.	ORDERS OF TM
PCV	1 504 098 590	$4,4	6,64E+09	377	376
HPV	119 428 050	$24,7	2,94E+09	186	186
Seasonal Influenza	824 789 746	$2,5	2,03E+09	272	107
Rota	753 220 702	$2,6	1,97E+09	211	205
Varicella	59 712 463	$19,8	1,18E+09	75	52
HepA	46 854 499	$12,3	5,74E+08	147	132
IPV	453 385 345	$1,0	4,67E+08	309	143
MenC conj.	39 889 215	$9,9	3,93E+08	35	31
bOPV	4 244 793 164	$0,1	3,7E+08	371	140
HepB	426 380 253	$0,8	3,29E+08	505	156
Hib	23 535 970	$9,0	2,12E+08	93	75
Measles	766 403 392	$0,2	1,63E+08	141	3
BCG	1 133 711 293	$0,1	1,23E+08	390	0
YF	298 440 401	$0,4	1,21E+08	172	104
JE	103 698 472	$0,9	95493823	37	5
PPSV	10 402 898	$8,3	86859914	76	76
Rabies	10 047 143	$6,8	68064082	94	76
TT	352 848 882	$0,1	49414440	143	25
tOPV	252 076 883	$0,1	20286958	53	34
Typhoid Ps	1 354 606	$3,9	5270656	37	28
TBE	455 155	$6,3	2866713	31	20

TABLE 4B. Summary table of vaccines' quantity, revenue, and mean price.

VACCINE	LIC	LMIC	UMIC	HIC	TOTAL OBS.	% OF TOTAL
BCG	77	119	124	70	390	11,60%
bOPV	113	138	97	23	371	11,00%
HepA	0	7	37	103	147	4,40%
HepB	12	117	185	191	505	15.0%
Hib	0	5	29	59	93	2,80%
HPV	19	21	55	91	186	5,50%
IPV	65	100	88	56	309	9,20%
JE	4	13	9	11	37	1,10%
Measles	56	47	33	5	141	4,20%
MenC conj.	0	0	2	33	35	1,00%
PCV	68	108	91	110	377	11,20%
PPSV	0	6	13	57	76	2,30%
Rabies	0	10	38	46	94	2,80%
Rota	50	78	42	41	211	6,30%
Seasonal Influenza	0	25	120	127	272	8,10%
TBE	0	1	10	20	31	0,90%
tOPV	8	27	17	1	53	1,60%
TT	38	43	39	23	143	4,20%
Typhoid Ps	0	2	8	27	37	1,10%
Varicella	0	0	25	50	75	2,20%
YF	43	43	52	34	172	5,10%
TOTAL	553	910	1114	1178	3755	100%

TABLE 5B. Summary table of vaccine purchases per income group.

VACCINES	PCV		HPV		Seasonal Influenza		Rota		Varicella	
VARIABLES	*logP*	*P*	*logP*	*P*	*logP*	*P*	*logP*	*P*	*logP*	
Q	-2,21E-09	0,999	-2,42E-08	0,994	-3.12e-09	0,999	-4,53E-09	0,999	-7.51e-09	0,998
	(8.14e-10)		(1.27e-08)		(1.98e-09)		(1.45e-09)		(9.48e-09)	
PQ	0,0799	1,202	-0,369	0,428	0,0845	1,215	0,535	3,428	0.0126	1,029
	(0.0272)		(0.0796)		(0.0415)		(0.0705)		(0.0512)	
SP	0,416	2,606	0,375	2,371	0,148	1,406	0,193	1,560	0,233	1,710
	(0.0363)		(0.0516)		(0.0336)		(0.0587)		(0.0335)	
LMIC	0,0739	1,185	0.0266	1,06	-	-	-0.00147	0,997	-	-
	(0.0208)		(0.0378)		-		(0.0255)		-	
UMIC	0,427	2,673	0,234	1,714	0.00901	1,021	0,316	2,070	-	-
	(0.0401)		(0.0363)		(0.0491)		(0.0452)		-	
HIC	0,671	4,688	0,501	3,170	0,205	1,603	0,771	5,902	0,111	1,291
	(0.0412)		(0.0636)		(0.0521)		(0.0704)		(0.0426)	
Constant	0,451	2,825	1,065	11,614	0,349	2,234	-0,132	0,738	1,12	13,183
	(0.0312)		(0.0828)		(0.0465)		(0.0749)		(0.0249)	
Observations	377		186		272		211		75	
R-squared	0.846		0.708		0.304		0.748		0.342	

TABLE 6B. Regression 2 conducted on the five vaccines generating the most revenue, including P.