Received: 2 May 2023 | Revised: 6 October 2023 | Accepted: 10 October 2023

DOI: 10.1111/twec.13533

ORIGINAL ARTICLE

The World Economy WILEY

The international trade in human vaccines before COVID-19

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Funding information
Consolidated Group of Research, Grant/Award Number: 2014-SGR-1395; H2020 Marie Skłodowska-Curie Actions, Grant/Award Number: 713679; PNRR – GRINS – GROWING RESILIENT, INCLUSIVE AND SUSTAINABLE (cod. PE0000018), Grant/Award Number: H73C22000930001; Universitat Rovira i Virgili, Grant/Award Number: 2019PFR-URV-B2-80

Abstract

The recent COVID-19 pandemic has highlighted the importance of global access to human vaccines. There is, however, no empirical work on either the unequal distribution of international trade or on its determinants. Applying a gravity model to the UN Comtrade database between 2000 and 2019, we explain the patterns of bilateral trade across 116 countries. Using the Poisson Pseudo-Maximum Likelihood methodology, our results show that inequalities in international vaccine trade have steadily increased. In general, supply and demand drivers play a role in explaining the flow of human vaccines. The impact of these drivers varies depending on the income level of the importing country. High-income countries intensify their flows with demand factors such as GDP per capita, or supply factors such as the location of big pharmaceutical companies. Conversely, low-income countries receive more vaccines according to their population. Our results show that a poor country that houses a big pharmaceutical company acts as an exporting platform to developing and poor countries. Middle-income countries present features similar to rich countries both by producing more and also by exporting more. The imbalance endangers the global fight against the current COVID-19 pandemic.

KEYWORDS
bilateral trade, COVID-19, global inequalities, human vaccines

1 | INTRODUCTION

The dramatic consequences of the COVID-19 pandemic on worldwide health and economic activity forced pharmaceutical companies and governments to develop vaccines to inhibit the spread of the virus. In parallel, the World Health Organisation (WHO), non-profit organisations and private foundations encourage governments to join the Vaccine Global Access Facility (COVAX Facility) to ensure that vaccine doses were distributed to the most vulnerable populations (Emanuel et al., 2021).[1] However, there is still very unequal access to vaccines depending on a country's level of income and the strength of its health system (Agarwal & Gopinath, 2021) and the COVAX initiative itself has proven to be a huge failure (Bown & Bollyky, 2022).[2] Furthermore, only relatively few countries have the capacity to produce vaccines.[3] Hence, it is essential to explore the trends in global trade in human vaccines to try to eradicate pandemics but paying particular emphasis to the role of the supply and demand characteristics.

This paper explores the drivers of international trade in human vaccines during the period 2000–2019, paying particular attention to the differences in the determinants among three clusters of countries: OECD members (high-income countries), middle-income countries, and low-income countries.[4] Despite the relevance of the topic and the proliferation of studies on the COVID-19 pandemic, to date, the literature on bilateral trade in human vaccines between countries is sparse (Narayan, 2021). Equitable global distribution of vaccines is an ethical and humanitarian responsibility for developed countries and one which also results in significant economic benefits for the world economy. Thus, if we want to minimise the economic costs of pandemics, a coordinated worldwide push is required to produce and distribute vaccines (Cakmakli et al., 2021). Although, in an unprecedented effort, the big pharmaceutical companies have produced many effective vaccines in a short time,[5] the dose distribution in lower-income countries has been low. Therefore, understanding the drivers of worldwide trade in human vaccines is necessary for successfully distributing COVID-19 vaccines globally.

To undertake this study, we used the bilateral flows of human vaccines from the Trade Statistics Database (UN Comtrade) for nearly 200 countries over the period 2000–2019. After data cleansing, our final sample contains bilateral human vaccine flows for 116 countries

[1]COVAX is co-led by Gavi (the Vaccine Alliance), the Coalition for Epidemic Preparedness Innovations and the World Health Organisation (WHO) and aims to ensure fair and equitable access to every country in the world. COVAX aims to guarantee an equitable distribution of the vaccine between countries. As of January 2021, 190 countries are committed to COVAX.

[2]Despite the global dimension of COVID-19, by the end of 2022, only 22.3% of people in low-income countries had received at least one dose (Our World in Data).

[3]The vaccine industry is capital intensive and requires substantial ongoing investment in manufacturing assets, facilities, and trained people for research, product development, manufacturing, and compliance with regulatory directives. The components of the human vaccine industry are dispersed among 50 countries worldwide. The largest vaccine companies are in the United States or the European Union, although regional companies are gradually growing their market share in international trade (Douglas & Samant, 2018).

[4]We do not distinguish between the terms "high-income" and "developed" countries for OECD member countries, while we divide developing countries into two groups: the "middle-income" and the "low-income" countries. We also refer the latter as "poor" countries.

[5]The COVID-19 global pandemic has made the development of vaccines necessary to increase population immunity by stimulating the production of antibodies against the infection. As of October 2021, 23 vaccines had been accepted by the competent authorities and 429 were in the testing phase. Some studies estimated the cost-effectiveness of vaccination, with very favourable results, suggesting that vaccines against COVID can reduce healthcare costs by up to 60% (López et al., 2021).

representing more than 95% of the world's population. Of these, 34 countries belong to the OECD, 38 to middle-income countries, and the remaining 44 to the low-income country group.[6] At the methodological level, we apply a Poisson Pseudo-Maximum Likelihood (PPML) estimation method proposed by authors such as Larch et al. (2019) and Santos Silva and Tenreyro (2006).

Our empirical results identify the influence of some drivers related to the demand and supply of human vaccines (such as production specialisation in the pharmaceutical industry, and international competitiveness or the market dimension). Furthermore, our results show that the drivers of such international trade differ across the three groups of countries. In particular, high-income countries intensify their flows with demand factors such as GDP per capita or supply factors such as the location of big pharmaceutical companies. Conversely, low-income countries receive more vaccines in line with their population. Our results show that a poor country hosting a big pharmaceutical company plays the role of an exporting platform. Middle-income countries present features similar to rich countries by both producing and exporting more.

As far as we are aware, there are no similar empirical works analysing the international trade of human vaccines. This should not be surprising since studies on bilateral trade drivers in pharmaceutical products have received little attention. Among previous studies, we note those of Smith (2002), Boring (2010), Blanc (2015) Joshi (2015) and Lee and Yun (2018). For instance, Smith (2002) shows the importance of patents on the trade flows of biological products. Blanc (2015) analyses the determinants of EU exports of pharmaceutical products. Finally, Lee and Yun (2018) analyse the global pharmaceutical value chain in South Korea. Our study contributes to the analysis of the supply and demand drivers of the international trade of a specific pharmaceutical product. Our approach captures the effect of a highly concentrated supply together with a highly dispersed demand having unequal access to human vaccines. Furthermore, our research shows how traditional variables such as the territorial proximity and the existence of free trade agreements are less important for low-income countries that are net importers. Our results question the capacity of traditional trade models to explain the international trade of products highly controlled by large pharmaceutical corporations.

From a policy point of view, our results show that poor and rich countries have different drivers of international trade which lead to an unequal distribution of vaccines across the world. Consequently, the market-driven paradigm seems insufficient to address the unequal effects of COVID-19 across social groups, income levels, and countries. This suggests that the development of more ambitious vaccination strategies may help to control the current pandemic. For instance, there is a need to establish resources and productive capabilities for mature vaccines in developing countries and there will undoubtedly be an overall growth in the human vaccine market over the next few years. This is an important issue since we cannot ignore the fact that vaccination programs will only achieve herd immunity when a high proportion of the population is vaccinated (Neumann-Böhme et al., 2020), especially in cases like COVID-19 where the rate

[6]During the period under study, the three groups show clear differences in their international trade patterns. OECD member countries accounted for 98% of worldwide exports (Belgium, Ireland, France, United States, United Kingdom, among others); middle-income countries such as India, China, and Singapore exported mainly to less developed countries which, in turn, acted as net importers thanks to support from international health agencies. Most developing countries are net importers. Developed countries absorb 85% of world vaccine imports, while developing countries receive only the remaining 15% (Source: own elaboration from UN Comtrade).

of infection and the severe symptoms create a risk of collapse for health systems in some countries. More generally, as suggested also in Zimmermann et al. (2020), trade policies can and shall be devised to improve a widespread exchange of goods and services aimed at fighting diseases instead of damaging it.

This paper is organised as follows. Section 2 reviews the patterns of international trade in human vaccines. Section 3 presents the main theoretical and empirical literature on the pharmaceutical industry and bilateral trade. Section 4 describes the database and our econometric methodology. Section 5 contains the results obtained, and, finally, Section 6 provides our main concluding remarks.

2 | PATTERNS OF INTERNATIONAL TRADE IN HUMAN VACCINES

The international trade in human vaccines has specific features, which are summarised as follows. First, it is a high-growth market. Global exports of human vaccines amounted 31.7 billion US $ in 2019. During the period 2015–2019, the human vaccine trade increased by 19.8%, and the COVID-19 pandemic will undoubtedly cause considerable further growth. Second, the market is highly concentrated. In 2019, European suppliers accounted for 87.5% of global human vaccines exports, North American exporters 7.8%; Asian exporters 4.3% and Oceania 0.3%, while other areas exported negligible amounts. Third, low-income countries participate less in the international trade of human vaccines. During the first decade of the 21st century, flows of vaccines to countries with the lowest per capita income increased, but the flows decreased after the 2008 crisis. Fourth, the vaccine trade has become a regional trade, where pharmaceutical firms located in some developed countries invest substantial amounts in R&D to develop human vaccines for these markets. Consequently, the trade of human vaccines among OECD countries has grown, while remaining stable or decreasing between developed and developing countries.[7]

Overall, the global trade of human vaccines between countries shows persistent imbalances that are related to per capita income. First, although the populations with the highest exposure risks live in countries with low per-capita income, the global market for vaccines continues to be concentrated in a few developed countries (Jadhav et al., 2014).[8] Second, developed countries purchase the most expensive and modern human vaccines, while low-income countries suffer a high impact from diseases preventable by vaccination. Third, there is an unequal distribution of production, which causes international dependence (Sorescu et al., 2021). Despite WHO programs to promote global vaccine production capacity, OECD countries are net exporters of human vaccines, while many developing countries import doses of human vaccines designed to immunise their local population (Table A1 in Appendix 1). Fourth, a group of strong suppliers in emerging economies such as China, Brazil and India has appeared. Their success is mainly

[7]According to the Global Forum for Health Research, only about 10% of global spending on US health R&D went to research on 90% of the world's health problems. The 10/90 ratio reflects a broader problem best described as the growing number of "underserved populations". This problem has increased in recent years as large pharmaceutical corporations invest increasing R&D resources in the development of vaccines for developed countries, to the detriment of diseases that predominantly affect developing countries, the "neglected diseases" (Viergever, 2013).

[8]According to the UN Comtrade dataset, during the period 2000–2004, OECD member countries accounted for 96.33% of global exports (73.66% of imports) in current dollars. For the period 2014–2018, the corresponding figures were 96.08% of exports (80.14% of imports).

TABLE 1 Bilateral trade of human vaccines (2000–2019).

Level of income in the country according to the World Bank			Importing countries: Absolute values (millions $) High	Medium	Low	Relative values of supply High	Medium	Low
Exporting countries	Absolute values	High	235,000	31,900	16,900	83%	11%	6%
		Medium	114	953	1940	28%	24%	48%
		Low	513	1230	3340	10%	24%	66%
	Relative values of demand	High	99.3%	93.6%	76.2%			
		Medium	0.5%	2.8%	8.57%			
		Low	0.2%	3.6%	15.1%			

Note: Table A2 in Appendix 1 contains a complete list of countries per cluster. Source: Own elaboration from UN Comtrade. N.B. The data on the three income groups cover 98% of world exports (and 99% of world imports) of human vaccines.

TABLE 2 Average trade price (in thousands of dollars per kilo) of human vaccines for the clusters.

Export		Import	
Income cluster	**Average price**	**Income cluster**	**Average price**
2019			
High	0.713	High	0.724
Medium	0.419	Medium	0.619
Low	0.311	Low	0.49
2000			
High	0.301	High	0.703
Medium	0.169	Medium	0.190
Low	0.080	Low	0.095

Source: Own elaboration from WITS data.

attributable to the development of an intellectual property system that significantly reduces production costs while achieving the strict quality controls mandated by international organisations (Milstien et al., 2007).

Finally, there is a clear imbalance between demand needs and private incentives (Ganslandt et al., 2001). Human vaccine producers have few incentives to develop products with low commercial margins (Offit, 2005; Rovira, 2002).[9] There are several reasons for this. First, human vaccines are usually a single dose (or at most a few). Second, the demand for these low-margin vaccines is uncertain and depends on the results achieved during the vaccination campaigns. Finally, the vaccine demand in developing countries also depends on the decisions taken by the WHO, UNICEF, or non-profit organisations in their immunisation programs (Milstien & Kaddar, 2006). Consequently, since rich markets can pay higher prices, the R&D costs for the development of new human vaccines have increased. These higher prices in developed countries work to the detriment of social responsibility for the population most affected by diseases in developing countries (Plotkin et al., 2017).

To sum up, the international trade of human vaccines is characterised by the concentration of supply (see Table A1), while there is a dispersion of demand.[10] To shed more light on these features, Table 1 presents the absolute values of trade for our three country clusters. We distinguish between relative values according to the final markets (percentage of supply) and the share of the origin of the imports for each group (percentage of demand). Our results show that high-income countries act as final markets. This confirms that rich countries mainly produce high-price, high value-added, products intended for countries that are also rich. Conversely, emerging countries

[9]Stern and Markel (2005) stated that "many pharmaceutical companies avoid the vaccine business because it is economically prohibitive and encumbered by regulatory barriers."

[10]An additional non-negligible factor that may affect the asymmetrical distribution of vaccine producers has to do with the issue of tax heavens. Indeed, given the large presence of multinational enterprises in the pharmaceutical industry, it may be that some of these locate in tax-favourable countries. In this, the leading example might be Ireland, whose policies attracted many inward FDIs, especially in the pharmaceutical sector (Van Egeraat & Barry, 2008). Nevertheless, we stress how taking these complex relationships into account might divert excessively the focus of the analysis. Further, in the analytical framework that we developed, a company that chose Ireland because of the above reasons, has very likely chosen it to access the larger EU market, and if not there, it would have still located within a high-income country.

mainly trade with poor countries. Interestingly, we observe diverse markets where buyers and sellers exchange differentiated goods.

Regarding the relative values of demand, the results reveal a high dependence of all countries for vaccine production originating in rich countries. The most extreme data belongs to the rich countries (a 99.3% share), while low-income countries have a relatively high share of trade in low-income countries. Therefore, despite a high share of the vaccines produced in low-income countries having other low-income countries as their final market, this production is not enough to satisfy their needs.[11]

Finally, the information provided by the World Integrated Trade Solution (WITS) allows us to observe the evolution of vaccine prices in world trade. Table 2 confirms two facts that we have been highlighting. On the one hand, the average price for exported and imported vaccines varies considerably according to the income cluster, being lower in low-income countries. This evidence suggests that newly developed vaccines tend to be manufactured in rich countries, while the more standard ones are produced in the remaining countries. On the other hand, during the period 2000–2019, the prices of human vaccines increased much more among low- and middle-income countries. These results are consistent with the studies by the WHO (2019) when they analyse the determinants of vaccine prices by levels of income per inhabitant during the period 2013–2017 and observe that countries with low levels of GDP per capita register strong price increases in human vaccines, while higher-income countries experience smaller increases in vaccine prices.

This evidence shows that the international trade of human vaccines is unbalanced and mainly concentrated among developed countries. Hence, it is necessary to understand the drivers that generate this phenomenon. The following section presents theoretical and empirical arguments explaining the drivers of the international trade of human vaccines.

3 | LITERATURE REVIEW: DEMAND AND SUPPLY DRIVERS OF VACCINE TRADE

The pattern of international trade may be the result of the interaction between geographical and cultural aspects, trade agreements and the characteristics of the location of supply and demand of a product. From a supply–demand side, the drivers of low-profit markets such as vaccines can be grouped into "push" and "pull" forces (Milstien & Kaddar, 2006). In essence, a human vaccine is developed either because of a clear demand (a "pull demand force"), or because it becomes technically and operationally feasible (a "push supply force"). This section presents the demand and supply determinants, which may affect the pharmaceutical trade and, in particular, that of human vaccines.

3.1 | Demand drivers

Demand forces are crucial in explaining the bilateral trade in human vaccines. Blanc (2015) shows that the main drivers are the protection of intellectual property in the final countries, the

[11] Appendix 2 highlights the heterogeneity of the international trade of human vaccines across countries (Table A7). The results for skewness and kurtosis (Table A8) are highly concentrated regardless of whether we consider the intensive margin or the number of markets. However, the skewness analysis is not significant for the period 2009–2019.

economic size of final markets, the importance of their health sector, and the quality of their infrastructures. On the one hand, there is evidence that the vaccine market is stratified by income segment (Cernuschi et al., 2020). In 2017, high-income countries accounted for 56% of the total market value, followed by the middle-income country market at 26%. Furthermore, middle-income countries received little financial support from donors for vaccine purchases, limited vaccine price or market information, thus hampering their ability to negotiate equitable prices. Conversely, low-income countries received financial support for low-priced purchase of vaccines. Most middle-income countries have two challenges: they are slow to introduce new vaccines and, in some cases, lag behind in the coverage of traditional vaccines.

On the other hand, the development of health systems in each country constitutes one of the most relevant "pull demand forces" in the global vaccine market. The health system expenditure affects vaccine demand. Countries with a strong health system will ensure domestic demand for medical goods and facilities, whereas poor countries lack the resources to become active participants in this international trade. An extremely low (or non-existent) level of investment in public health is a key characteristic of poor countries, which often rely on WHO and UNICEF campaigns. This factor becomes relevant in the human vaccine context, as does the location patterns of vaccine manufacturers and the specific industrial and technological production skills needed.

Furthermore, the development of new vaccines depends on market size. For instance, using US and OECD data, Acemoglu and Joshua (2004) investigate the effect of market size on drug entry and pharmaceutical innovation. Their results show that the development and launch of new drugs are susceptible to standard economic explanations such as market size. Furthermore, they show the reaction to the entry of non-generic drugs, "which correspond more closely to new products and innovation."

Therefore, we expect that the development of health systems and increasing market size foster international trade in human vaccines across countries. Taken together with those drivers related to the stalling of human vaccine consumption attributable to the national health system and the national market in general, we are consider a series of forces promoting the development of human vaccines linked to the features of the pharmaceutical industry.

3.2 | Supply drivers

While the demand for human vaccines is global, their production is likely to be geographically concentrated (OECD, 2021). Lee and Yun (2018) show that the pharmaceutical value chain is heavily regional, where European countries are positioned as a first-tier supplier and the Asian region as the second-tier supplier. The development and production of human vaccines are highly concentrated according to the comparative advantages of each country and their specialisation.

Among production capacity determinants, R&D processes act as a "push supply force" for low-profit vaccine markets since countries with stronger innovation systems facilitate the production of higher added-value pharmaceutical products. Consequently, having a stronger R&D and innovation system is an important incentive for private companies. Furthermore, the connection between public basic research and the development of new medicines is also clear. Cohen et al. (2002) reported that public research influenced new project ideas in the pharmaceutical industry more than in any other manufacturing industry. Similarly, Toole (2012) showed that public basic research usually plays a crucial role in the earliest stage of pharmaceutical drug discovery and fosters the entry of new drugs. As Plotkin (2005) points out, a consequence is that, if manufacturers see scaling up and producing a particular vaccine deriving from academia or a biotech firm as problematic, it will quickly be abandoned.

Conversely, having a robust R&D system is a necessary, but not sufficient, condition for exporting pharmaceutical products. In the pharmaceutical industry, accumulated experience and learning are huge advantages for production and internationalisation activities (Malerba & Orsenigo, 2015).[12] Hence, technological spillovers from robust scientific, technological, and innovative systems and universities are the fundamental determinants for the location of large companies' research centres (US, Germany, and France, among others). However, Milstien and Kaddar (2006) worry that strong IPR protection could also be a barrier to accessing future vaccines and Smith (2002) confirms the influence of patents on the trade flows of drugs for the USA.

Therefore, this causes a division in the production of high added-value vaccines in countries with intense R&D investment, and the production of low added-value vaccines in countries with weak innovation systems. The result is a fragmentation of production, which has facilitated some developing countries (India, Singapore and Indonesia) in becoming large-scale vaccine manufacturers, while international vaccine trade remains concentrated in a few logistic hubs. These countries are both major exporters and importers of human vaccines. Thus, the relationship between demand (import) and supply (export) of human vaccines necessarily differs between developed and developing countries. As described by Melitz (2003) and Helpman et al. (2004), international trade between firms located in different markets may explain the expansion of the pharmaceutical industry among countries and the intra-industry trade growth among countries.[13]

Finally, the extension of intellectual property rights abroad has also facilitated the growth of international trade in human vaccines (Pore et al., 2008), together with a higher interest in searching for market opportunities abroad. We expect that countries specialised in pharmaceutical activities will generate virtuous cycles that facilitate the production and export of human vaccines.[14]

Finally, we must also consider the relative (dis)advantage in terms of a country's endowment as compared to its peers. International trade has been traditionally explained by differences in factor endowments. More recently, the New Trade Theory demonstrated the existence of intra-industrial exchanges, particularly among more similar countries. Indeed, trade growth had also been strongest between countries that were similar to each other in size, factor endowments and comparative advantage. Regardless of their emphasis in explaining inter- or intra-industrial trade, these theories highlight the existence of trade imbalances. At theoretical level, Shen et al. (2022) show the importance of the inherent dynamics between the factor endowment

[12]Malerba and Orsenigo (2015) present an evolutionary approach to the traits of the pharmaceutical industry. This is characterised by the historical evolution of different agents due to the adaptation to knowledge and the technological context, firms' strategies, demand, and institutional frameworks.

[13]Despite not being the aim of the article, we should point out that the COVID-19 pandemic has modified the strategies of multinationals (Antràs, 2020) and will alter global value chains (Strange, 2020). COVID-19 may have also affected the production fragmentation developed by multinationals producing vaccines.

[14]Since vaccine production belongs to the pharma industry, we can think that there is a certain endogeneity between these sectors. Consequently, the general trade in the pharma industry may condition the vaccine industry (which, however, represents a relatively small proportion of the pharma industry). As pointed out by Douglas and Samant (2018), in the past 20 years, the vaccine sector, previously a mature sector in the pharmaceutical business, has shown remarkable growth fuelled by innovative new vaccines coupled with superior pricing strategies. The evolution of trade in any particular small share sector, may not condition the evolution of the pharma industry as a whole.

structure of Southern countries and global trade imbalances. Interestingly, their model implies that trade imbalances may evolve over time according to the factor endowment of each country. As shown in Section 2, the evidence suggests imbalances in the trade of human vaccines, but also we observe a change driven by the appearance of new-incoming countries producing and exporting. Hence, it is necessary to analyse the interrelations among countries according to the type of flow and their characteristics.

4 | DATA SOURCES AND ECONOMETRIC METHODS

Our analysis is based on the bilateral trade flow data compiled by the United Nations Statistical Division in the Comtrade database.[15] The data span the period 2000–2019, cover nearly 200 countries, and report bilateral trades for over six thousand goods, classified according to the Standard International Trade Classification and the Harmonised System (HS), which can be broken down to the 6-digit level. For our purpose, we use the HS classification.

We focus on a specific 6-digit product: 300220, human vaccines. In addition, we restrict the sample to those countries with populations greater than 1.5 million inhabitants to reduce biases due to a lack of data. Furthermore, we categorise countries into three clusters: OECD or high-income countries (34 countries), middle-income countries (38 countries), and low-income countries (44 countries). Table A2 in Appendix 1 contains a complete list of countries per cluster. Additionally, we match the international trade values with different geographical and socio-economic data from a small number of validated sources. First, we include distances, common languages, and borders from the GeoDist database, compiled by CEPII. To this, we add data regarding countries' population and Gross Domestic Product (GDP) from the World Bank Database. Finally, for the model extensions, we also merge data regarding the achieved COVID-19 vaccination rate, and on the presence of big pharmaceutical companies, as reported by the Top2500 R&D investor scoreboard by JRC-Seville. Table A3 in the Appendix 1 summarises the sources and definitions of each variable. After these refinements, our sample has more than 58,000 observations of global bilateral trade of human vaccines relative to 2000–2019 and the associated country-level information, varying both by country and by year. The final data set includes 116 countries which together account for 99% of exports and 98% of world imports of human vaccines.

Concerning the empirical methodology, we exploit recent developments in the field of gravity models. They arise from Newton's Law of Gravity, which states that the gravitational attraction between two objects is positively related to their masses and inversely related to the squared distance between them. In its current form, following Feenstra (2015), the standard gravity equation can be log-linearised as follows:

$$X_{ijt} = exp\left(\alpha + \beta_1 \, lnGDP_{it} + \beta_2 \, lnGDP_{jt} + \beta_3 \, lnD_{ij} + \eta_i + \theta_j\right) + \upsilon_{ij} \quad (1)$$

where X_{ijt} are the exports from country i to country j, GDP corresponds to the Gross Domestic Product (GDP) of countries i and j, and D is the geographical distance between the two countries. η_i

[15]Specifically, we rely on The Growth Lab at Harvard University: International Trade Data (2019) version of the data, which applies a cleaning process, known as Bustos-Yildirim method, with the aim of increasing the consistency and reliability of trade flows by combining export and import information.

corresponds to an exporter fixed effect, θ_j is an importer fixed effect, and υ_{ij} is an error term. In the empirical estimations, usually the β_1 and β_2 parameters are positive and β_3 has a negative sign.

To the above, we add a set of explanatory variables aimed at capturing the supply and demand determinants that influence vaccine global trade. Specifically, our final equation takes the following form:

$$\begin{aligned} X_{ijt} = \; & exp(\alpha_0 + \alpha_1 DIST_{ij} + \alpha_2 COMMON_{ij} + \alpha_3 BORDER_{ij} + \alpha_4 FTA_{ijt} + \alpha_5 POP_{it} + \alpha_6 POP_{jt} + \alpha_7 GDPpc_{it} \\ & + \alpha_8 GDPpc_{jt} + \alpha_9 MORE\_VAX_{it} + \alpha_{10} GLindex_{it} + \alpha_{11} PHARMA\_PROD_{it} \\ & + \alpha_{12} PHARMA_{it} + \alpha_{13} PHARMA_{jt} + \alpha_{14} SIMILAR_{ijt} + \lambda_t) + \varepsilon_{ijt} \end{aligned} \tag{2}$$

where α are the parameters to estimate, λ_t is the time trend, ε corresponds to the error term, and X_{ijt} are the vaccine exports from country i to country j in year t expressed in current US$. As control variables we have *DIST*, which is the distance in kilometres between the capitals of a pair of countries, and *COMMON* and *BORDER* take a value equal to one if the countries share the same official language or a common border. Finally, we include a time-variant dummy variable *FTA* that tracks whether the country-pair enters into one of the free trade agreements of the WTO. The introduction of FTAs accounts for endogenous economic integration agreement formations (Bergstrand et al., 2015). As proxies of demand drivers, we include *POP*, which denotes the population of each country, and *GDPpc*, which is the income per capita (current purchasing power parity, US$ per thousand inhabitants) of countries i and j, respectively. These explanatory variables correspond to our baseline model.

The variable *MORE_VAX* exploits the recent COVID pandemic to proxy for vaccine demand with data on the recent COVID-related campaign. *MORE_VAX* takes the value of one if vaccines are flowing from countries with high rates of COVID-19 vaccinations (>70%) to countries with low rates (<40%).[16] It is a binary and it takes the value of 1 if the previous condition holds. Thus, if we find it positive and significant, it means that vaccine exports go from countries with highly vaccinated population to those ones with low rates.

Departing from this baseline model, we include different sets of variables to analyse our hypotheses. First, *GLindex* is the Grubel and Lloyd index of human vaccines in the exporting country. This variable measures the existence of intra-industry trade in the market.[17]

Second, a vector of determinants captures the demand and supply of human vaccines. On the one hand, in terms of potential supply proxies, we include a *PHARMA_EXP* and *PHARMA_IMP* variable, corresponding to the share of pharmaceutical exports over total trade between exporters and importers, and *PHARMA_PROD* variable, which takes the value of 1 if the exporter has a pharmaceutical company[18] located in it while the importer does not. Ideally, when significant, if negative this variable reinforces the idea of rich, technologically-advanced countries mostly

[16]For the sake of robustness, we moved the threshold with no significant changes in the coefficient estimates. Results are available upon request to the authors.

[17]The index takes values in the range 0 to 1 and is estimated by the following equation: $GL_{it} = \frac{(x_{it}+m_{it}) - |x_{it}-m_{it}|}{(x_{it}+m_{it})} = 1 - \frac{|x_{it}-m_{it}|}{(x_{it}+m_{it})} = \frac{2Min(x_{it};m_{it})}{(x_{it}+m_{it})}$, As can be seen in Table A6 in Appendix 1, inter-industry trade predominates in global human vaccine trade since only 15.8% of the 59,986 observations included in our database register bilateral trade between two countries. Furthermore, the Gruebel and Lloyd index of these intra-industry flows averages 0.256 and derives mostly from developed countries. Indeed, Table A6 in Appendix 1 shows that reciprocal trade in vaccines is concentrated in European countries.

[18]One which appears in the top 2500 global R&D investors.

exchanging among themselves, while excluding poorly-equipped countries which do not have big pharma companies. Finally, based on New Trade Theories, the variable *SIMILAR*[19] corresponds to the difference of the log GDP per capita between partner countries. This simple measurement captures the differences in the relative factor endowments between the two partners such as technology, skills, or education levels, but also captures consumer preferences.[20] All the explanatory variables, except the dummy variables, are in logs. See Tables A3–A5 in Appendix 1 for a description of the variables, their database sources, a statistical description, and a correlation matrix.

We must remark that, since we aim to capture time-invariant country dummies such as *DIST*, *COMMON* and *BORDER*, we have avoided including exporter-time and importer-time fixed effects. This might result in there being an omitted variable problem (because the impact of other time-variant country characteristics would not be captured). However, our dummy variables can capture unobservable multilateral resistances and time-invariant country characteristics. In this, it would be ideal to control for the presence of tariff and non-tariff measures affecting these flows. Nevertheless, their nature is extremely heterogenous in both numerosity and characteristics. The TRAIN database by UNCTAD (2023) reports more than 5000 measures active only in the 4-digit sector where vaccines are located, and a precise and rigorous inclusion of them in the modelling effort goes beyond the extent of the paper. Even if these regulatory acts tend to affect the availability, accessibility and affordability of vaccines in all countries (Gupta & Bhattacharjee, 2022), these practices are quite diffused, have normally "positive" aims, and they only partially affect a very long global value chain, made of shared practices, patents, routines, and ingredients.

Finally, the econometrics of the gravity equation has advanced in correcting biases that occur in estimates of trade flows between countries. Specifically, the issues concerning zero trade values and heteroskedastic residual have attracted debate (Martínez-Zarzoso, 2011). To address these issues, Santos Silva and Tenreyro (2006) show that PPML is more appropriate than the traditional OLS technique.[21] PPML assures maximum likelihood estimation convergence. Finally, PPML facilitates the inclusion of fixed effects for large data sets and allows for correlated errors across countries and time.[22] Also, with the aim of preserving the robustness of the *ppmlhdfe* estimator intact,[23] we did not drop any observation close to zero, and our sample has 40.1%, which is below the cautious thresholds tested by Martin and Pham (2020).

[19]This index is correlated with more insightful indexes such as the Economic Complexity Index, but is simpler in both formulation and interpretation.

[20]According to New Trade Theories, the scenarios are usually two. On the one hand, if the associated coefficient is positive, it implies that flows between countries with different GDP per capita are predominant. On the other hand, a negative relationship hints at an intra-industrial type of trade. Major differences in GDP per capita signal country pairs whose factorial endowments are quite different, and which would negatively affect the transaction. In this scenario, similar countries trade among themselves.

[21]The PPML estimator is robust for the analysis of nonlinear relationships in models where zero values are infrequent, as is our case (Martin & Pham, 2020).

[22]For a more complete explanation of gravity models see Yotov et al. (2016).

[23]The Stata package.

TABLE 3 Results of the PPML. Entire world. Dependent variable is the bilateral trade of human vaccines.

Variables	(1)	(2)	(3)	(4)	(5)	(6)
DIST	−0.242***	−0.239***	−0.225***	−0.202***	−0.245***	−0.217***
	(0.0594)	(0.0590)	(0.0598)	(0.0607)	(0.0584)	(0.0590)
COMMON	0.398***	0.397***	0.366***	0.405***	0.397***	0.355***
	(0.132)	(0.133)	(0.132)	(0.130)	(0.126)	(0.134)
BORDER	0.347***	0.350***	0.358***	0.342***	0.345***	0.374***
	(0.112)	(0.112)	(0.114)	(0.111)	(0.106)	(0.111)
FTA	−0.0159	−0.0138	−0.0283	0.0497	−0.0168	−0.0103
	(0.107)	(0.107)	(0.108)	(0.108)	(0.104)	(0.109)
POP_exporter	5.440***	5.441***	5.441***	5.572***	5.750***	5.555***
	(1.351)	(1.351)	(1.355)	(1.356)	(1.284)	(1.372)
POP_importer	−0.537*	−0.553*	−0.537*	−0.558*	−0.279	−0.640**
	(0.321)	(0.323)	(0.320)	(0.322)	(0.331)	(0.320)
GDPpc_EXP	1.052**	1.053**	1.071**	1.036**	0.699	1.191**
	(0.494)	(0.494)	(0.497)	(0.495)	(0.461)	(0.496)
GDPpc_IMP	0.340**	0.340**	0.337**	0.330**	0.403***	0.362**
	(0.148)	(0.148)	(0.148)	(0.148)	(0.139)	(0.153)
MORE_VAX		−0.205*				
		(0.123)				
GLindex			0.0277***			
			(0.0110)			
PHARMA_PROD				−1.527***		
				(0.175)		
PHARMA_EXP					0.931***	
					(0.109)	
PHARMA_IMP					0.0401	
					(0.0301)	
SIMILAR						−0.0872***
						(0.0314)
Constant	−78.67***	−78.43***	−78.85***	−80.29***	−81.40***	−79.90***
	(22.97)	(22.94)	(23.06)	(22.99)	(21.80)	(23.28)
Pseudo-R^2	0.8085	0.8086	0.8089	0.8101	0.8159	0.8094
Wald χ^2	1368.95	1383.49	1375.84	1503.47	1543.59	1540.39
Prob > χ^2	.0000	.0000	.0000	.0000	.0000	.0000
Observations	58,947					

Note: Time, export country and import country dummies are included. Robust standard errors in parentheses.
***$p < .01$; **$p < .05$; *$p < .1$.

5 | RESULTS

5.1 | Main estimates

This section contains the empirical results obtained from the gravity model presented above. Table 3 presents the estimates for all the country samples. Column 1 gives the baseline results for the main control variables. First, as expected, the distance between importer and exporter countries exerts a negative impact on trade.[24] Conversely, those countries sharing a common official language or contiguous frontiers present higher vaccine trade between countries. Variables such as the distance, the adjacency, and the use of a common language capture the effects of transport cost and costs of commercial transactions (Anderson & Wincoop, 2003; Bergstrand et al., 2015; Coe et al., 2007; Egger & Larch, 2012; Hou et al., 2023). Despite variables capturing the effects of distance (remoteness and land area) having diminished over time (Bleaney & Neaves, 2013), our analysis shows that these variables present the expected signs in human vaccines trade.

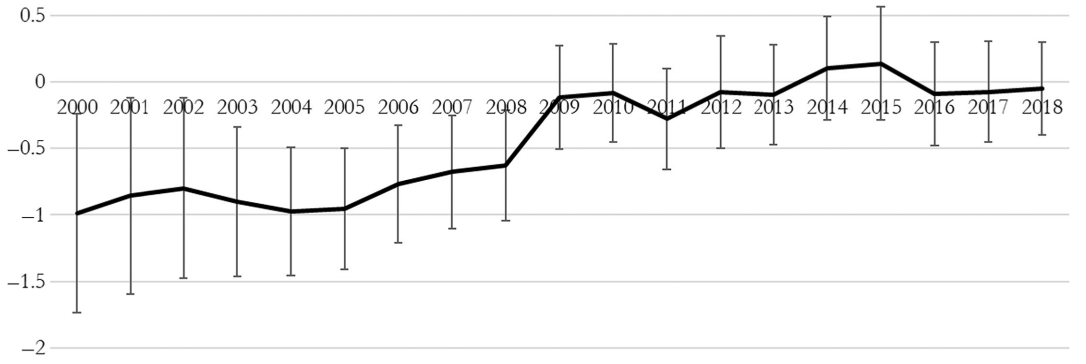
The incidence of Free Trade Agreements (FTAs) is non-significant and, therefore, presents ambiguous results when we consider trade between all the countries. It is widely accepted that economic integration agreements and other trade-policy liberalisations contribute to national economic growth and development, and help alleviate poverty. In general, the evidence shows that FTAs have substantially increased bilateral trade between member countries at the expense of the rest of the world (Spies & Marques, 2009). However, the nature of the traded products may cause the economic effects of such policies to vary depending on the economic structures of the countries (Baier et al., 2014). Hence, since human vaccines are characterised by a geographical concentration in production and by a dispersed global demand, FTAs may not be a determinant of their trade at global level.

Concerning those variables more related with the demand, in line with the literature, the bilateral trade of human vaccines is associated with the market size of the exporting and importing country. The international trade between countries is more intense when the population of the exporting country is higher, while highly populated importing countries seem to participate less intensively in the international trade of human vaccines. Furthermore, the GDP per capita is significant, not only for the exporting country, but also for the importing country. Hence, exporting countries are rich countries, but importing countries have also a larger GDP per capita. These results at global level indicate that income level is not only important for producing and exporting but also for importing. Conversely, the demand needs measured in terms of population, goes against expectation and indicates a certain unequal distribution. A deeper analysis in the next subsection may disentangle the effects of the income at country level.

Furthermore, the coefficient of the variable *MORE_VAX* (Column 2) exhibits a negative and slightly significant coefficient suggesting that, overall, vaccines do not flow from high-vaccination countries to low-vaccination ones. This result confirms that there is an unequal pattern of trade countries since more vaccinated countries do not trade so intensively with those that have weak health systems.

Concerning our proxies of supply, Column 3 incorporates our proxy for intra-industrial trade. The estimate shows a significant positive impact so, in our initial analysis, we prove the presence

[24]Some gravity-model studies found that the bilateral link between countries decreases with geographic distance, land area, and lack of access to the sea since these factors are correlated with transportation costs (Anderson & Wincoop, 2003; Coe et al., 2007). However, the effects of distance (remoteness and land area) have diminished over time (Bleaney & Neaves, 2013).



GRAPH 1 Estimated impact of the year coefficient in comparison with the year 2019. Vertical lines correspond to standard deviations. Lines not crossing the zero *y*-axis are statistically significant values.

of intra-industrial trade of human vaccines. Our results indicate that countries that import more intensively are those ones that also export more intensively. However, the low value of the coefficient may indicate a moderate role of trade hubs in the human vaccine market.

When we take into account the effect of the location of large pharmaceutical companies (Column 4), we notice how the strongly negative and significant estimate coefficient points to the idea that countries with consolidated pharmaceutical companies are less likely to trade intensively. Conversely, countries that does not have large pharmaceutical companies are confined to being less active in the international trade of vaccines.

In Column 5, we find an additional confirmation of the presence of supply forces. There, we measure whether specialisation in the pharmaceutical industry exerts a significant role in the international trade of human vaccines. The results demonstrate that such specialisation has a positive influence on the trade of human vaccines and particularly on that of exporting countries.

Finally, Column 6 incorporates our proxy for similarity in the endowments of the two countries (*SIMILAR*). The coefficient has a significant negative sign, showing that similar countries have greater bilateral trade in human vaccines, while dissimilar countries have less intensive trade.

Our results point to large producers mainly being located in rich countries with strong R&D systems and whose trade is low with low-vaccinated countries. All in all, rich countries mostly exchange among themselves, while excluding poorly equipped countries which do not have big pharma companies.

Regarding the estimates of time trend in our baseline model (Column 1 of Table 3), we observe that during the period 2000–2008, the trade flow of human vaccines was significantly lower than in the reference year 2019 (Graph 1). Furthermore, once we control for all the relevant variables, the coefficients show the trade of human vaccines increasing yearly. However, this trend changed in 2009, and our estimates for the second half of the period show that the time trend does not exert any significant impact. In line with Rodrigues and Plotkin (2020), this graph highlights the stagnation in human vaccine trade following the 2008 crisis.

5.2 | The influence of the income level of countries in the international trade of human vaccines

As pointed out in Section 2, both the demand and supply of human vaccines are complex. On the one hand, the demand for human vaccines differs according to the socioeconomic and technological characteristics of the countries involved. On the other hand, supply is concentrated in relatively few exporting countries. This section examines the extent to which the income-level of countries affects the determinants of supply and demand of vaccines. Table 4 shows the same estimates as Table 3 but classifies importing countries according to whether they are high-, medium-, or low-income countries.

For high-income countries, we confirm all our baseline results with two exceptions. The *MORE_VAX* variable is omitted because by construction, there are too small differences among the countries in the sample. Further, the variable *SIMILAR* is not significant, again due to excessive similarities among the countries in the high-income sample. Interestingly, *FTA* presents a significant and positive sign for high-income countries while this coefficient becomes negative for medium-income countries. This is a remarkable result given that rich importers benefit from the existence of FTA with exporter countries, while medium-income countries trade less intensively. This may be explained by the high concentration of production and also the different nature of FTAs in high- and medium-income countries.

Contrarily, the group of medium-income countries shows more heterogeneity in country characteristics. The market size of the exporter does not have an influence, while the population of the importing coefficient is a significant variable in determining the trade flow of human vaccines. This is an important result in comparison with the group of rich countries where the population coefficient was only significant for the exporting countries. Some further explanation of this is due. Among high-income countries, given that there are very few strong exporters and many importers, it derives from the fact that changes in population size among exporters are much smaller than among importers. For middle-income countries, the situation reverses, as the number of countries is more numerous, relatively wealthy and all have growing populations. All these factors trigger the possibility (and necessity) of importing more vaccines. Finally, among low-income countries, both population coefficients are positive and significant, as growing importing populations need vaccines (with financial aid from humanitarian campaigns) and the exporting population of pharmaceutical-producing countries such as India is steadily growing.

Continuing the discussion of the results, we should note that, for medium-income countries, sharing a common border and the GDP per capita of exporters are non-significant variables. Therefore, medium-income countries import from non-neighbourhood countries that are not necessarily richer. Additionally, medium-income countries' flows go from more human vaccinated countries to those with lower ratios (Column 10). The result highlights the role of medium-income countries as suppliers of human vaccines to low-vaccinated countries, which are likely poor countries.

In comparison with our main results our proxy of intra-industrial trade is significant and negative between medium-income countries (the greater the intra-industry trade, the lower the flow of human vaccines). Hence, for medium-income countries, we observe that the international trade of human vaccines is characterised by an intra-industry trade.

Nevertheless, if we look in-depth at pharmaceutical production, medium-income countries still exhibit a polarising trend where countries without strong producers struggle in provisioning vaccines. To alleviate the problem, medium-income countries import from countries with a high share of trade in the pharmaceutical industry (Column 11). Finally, the degree of similarity (Column 12) between the importing and exporting countries has a negative and significant coefficient. Recall our interpretation that similar countries have a greater bilateral trade in human vaccines, while dissimilar countries have fewer intensive exchanges. In this interpretation, middle-income countries tend to intensify their trade among countries which are more similar in terms of their endowments.

TABLE 4 Results of the PPML according to the income country classification (dependent variable = bilateral trade of human vaccines).

	High-income countries						Medium-income countries	
Variables	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**
DIST	−0.123	−0.123	−0.122	−0.0960	−0.115	−0.130	−0.283***	−0.281***
	(0.0854)	(0.0854)	(0.0852)	(0.0862)	(0.0841)	(0.0837)	(0.0678)	(0.0673)
COMMON	0.523***	0.523***	0.511***	0.534***	0.520***	0.559***	0.294***	0.306***
	(0.142)	(0.142)	(0.143)	(0.140)	(0.134)	(0.139)	(0.114)	(0.115)
BORDER	0.320**	0.320**	0.324**	0.312**	0.323***	0.297**	−0.255	−0.260
	(0.129)	(0.129)	(0.130)	(0.128)	(0.122)	(0.128)	(0.162)	(0.163)
FTA	0.145	0.145	0.132	0.199	0.179	0.150	0.526***	0.494***
	(0.160)	(0.160)	(0.166)	(0.164)	(0.156)	(0.158)	(0.0735)	(0.0756)
POP_EXP	6.483***	6.483***	6.479***	6.549***	6.499***	6.368***	0.399	0.390
	(1.606)	(1.606)	(1.609)	(1.610)	(1.545)	(1.589)	(1.431)	(1.433)
POP_IMP	−1.329	−1.329	−1.349	−1.306	−1.071	−1.365	0.962***	0.967***
	(0.974)	(0.974)	(0.979)	(0.975)	(0.992)	(0.964)	(0.327)	(0.327)
GDPpc_EXP	1.450**	1.450**	1.456**	1.442**	0.951	1.343**	0.259	0.262
	(0.647)	(0.647)	(0.649)	(0.646)	(0.620)	(0.640)	(0.281)	(0.281)
GDPpc_IMP	1.170***	1.170***	1.164***	1.158***	1.182***	1.099***	0.582***	0.584***
	(0.389)	(0.389)	(0.388)	(0.389)	(0.355)	(0.387)	(0.177)	(0.177)
MORE_VAX		-						0.293**
								(0.144)
GL index			0.0089					
			(0.0139)					
vax_productor				−1.624***				
				(0.234)				
PHARMA_EXP					1.132***			
					(0.132)			
PHARMA_IMP					0.0888			
					(0.0938)			
SIMILAR						0.0540		
						(0.0390)		
Constant	−95.99***	−95.99***	−95.53***	−97.41***	−90.67***	−91.89***	−13.12	−13.13
	(32.42)	(32.42)	(32.51)	(32.48)	(31.13)	(31.90)	(25.84)	(25.89)
Pseudo-R^2	0.8283	0.8283	0.8283	0.8292	0.8383	0.8285	0.7778	0.7780
Wald χ^2	995.99	995.99	997.54	1078.40	1089.27	1088.31	1540.08	1538.67
Prob > χ^2	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
Observations	27,799						14,950	

Note: time, export country and import country dummies are included. Robust standard errors in parentheses.
***$p < .01$; **$p < .05$; *$p < .1$.

Concerning the estimates for low-income countries, first, and contrary to the expectations of the trade literature, a common language and border contiguity have significant negative impacts. Additionally, the market size of exporters and importers exerts a positive and significant impact on the flow. Second, the intra-industrial proxy shows a non-significant impact which highlights

				Low-income countries					
(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)
−0.308***	−0.268***	−0.271***	−0.294***	−0.268***	−0.275***	−0.268***	−0.283***	−0.268***	−0.268***
(0.0675)	(0.0686)	(0.0696)	(0.0685)	(0.0697)	(0.0699)	(0.0699)	(0.0689)	(0.0693)	(0.0697)
0.326***	0.270**	0.308***	0.297***	−0.290***	−0.296***	−0.289***	−0.282***	−0.290***	−0.289***
(0.113)	(0.115)	(0.111)	(0.114)	(0.0841)	(0.0825)	(0.0840)	(0.0846)	(0.0841)	(0.0842)
−0.167	−0.273*	−0.241	−0.333**	−0.217	−0.145	−0.218	−0.165	−0.216	−0.216
(0.162)	(0.161)	(0.162)	(0.164)	(0.168)	(0.170)	(0.169)	(0.167)	(0.168)	(0.168)
0.523***	0.543***	0.540***	0.510***	0.0780	0.110	0.0779	0.00263	0.0770	0.0782
(0.0738)	(0.0738)	(0.0742)	(0.0723)	(0.123)	(0.123)	(0.123)	(0.101)	(0.122)	(0.123)
0.378	0.292	1.263	0.409	4.092***	4.063***	4.090***	3.975***	3.966***	4.095***
(1.409)	(1.415)	(1.368)	(1.433)	(1.143)	(1.138)	(1.144)	(1.092)	(1.154)	(1.138)
0.978***	0.962***	0.932***	0.948***	1.589***	1.566***	1.589***	1.583***	1.657***	1.589***
(0.325)	(0.328)	(0.328)	(0.330)	(0.411)	(0.410)	(0.412)	(0.411)	(0.418)	(0.411)
0.286	0.278	0.191	0.384	0.284*	0.278*	0.284*	0.324**	0.304**	0.280
(0.281)	(0.282)	(0.266)	(0.286)	(0.157)	(0.156)	(0.157)	(0.155)	(0.155)	(0.171)
0.605***	0.577***	0.572***	0.563***	0.000170	0.00359	0.000459	−0.00954	0.0126	0.000110
(0.177)	(0.176)	(0.175)	(0.176)	(0.113)	(0.113)	(0.112)	(0.111)	(0.113)	(0.113)
					−0.275***				
					(0.0977)				
0.040***						−0.0012			
(0.014)						(0.018)			
	−1.994***						0.861***		
	(0.370)						(0.277)		
		0.404***						−0.0306	
		(0.112)						(0.0883)	
		−0.0068						0.0197	
		(0.0308)						(0.0193)	
			−0.128***						0.0041
			(0.0349)						(0.0544)
−13.67	−9.881	−25.21	−12.78	−86.57***	−86.55***	−85.46***	−85.26***	−85.80***	−86.61***
(25.50)	(25.56)	(24.82)	(25.86)	(21.12)	(21.12)	(20.88)	(20.71)	(21.53)	(21.05)
0.7790	0.7789	0.7802	0.7785	0.6890	0.6898	0.6890	0.6913	0.6891	0.6890
1520.36	1537.92	1644.04	1544.81	1622.67	1640.89	1628.57	1651.70	1654.36	1673.49
.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
				13,393					

the role of low-income countries as mere buyers in the global market. All this evidence suggests that most poor countries around the world are highly dependent of the supply of vaccines from exporter countries. In other words, intra-industrial trade in human vaccines takes place between relatively few rich and middle-income countries, while the poorest ones have a trade deficit.

Another notable outcome is that most of our augmenting variables have their estimated coefficients flipped. Within this group of countries, vaccines flow from high-vaccinated countries to low-vaccinated countries.

6 | CONCLUSIONS

During the first two decades of the 21st century, low-income countries show a worrying reduction in the share of human vaccine trade, while developed countries have increased their share. Since 2008, market forces have increasingly dominated the research, development, manufacture and distribution of vaccines to the detriment of humanitarian goals. Accordingly, large pharmaceutical companies have reoriented their R&D activities towards searching for new vaccines for high-income countries, while the development of mature vaccines has languished. In this context, high-income countries acquire the most sophisticated and expensive vaccines, while the production of vaccines for classic diseases still present in developing countries stagnates. Hence, in the last two decades, the empirical evidence shows the increasing fragmentation of the international human vaccine trade.

In the light of the growing inequality in the international human vaccine trade, the current paper explores some of the determinants of the trade pattern and the differences between country groups. Applying a gravity model, our results shed light on some supply–demand determinants of these flows.

The above results allow us to reach a series of interesting conclusions. First, the standard explanatory factors for trade may not be adequate for explaining the human vaccine trade. For instance, sharing a common official language and contiguous borders are no longer significant for medium- and low-income countries. The main reason for this is that producers of human vaccines locate in developed countries (and some developing) countries. Second, high-income countries tend to export to high-income countries and developing countries; middle-income countries produce for developing countries, and low-income countries merely act as net importers with some notable exception. Nevertheless, the dominating behaviour of high-income countries is far from being inclusive. Additionally, the traditional instruments to promote the international trade among regions are not effective in explaining the human vaccine trade. Trade agreements seem to be effective only for high-income countries, but not for low-income countries. Finally, our results also show that trade had been continuously increasing up to the global economic crisis of 2008 when it began to stagnate.

Concerning the demand drivers, the population size is a key variable to explain the flow of human vaccines for medium- and low-income countries. Conversely, the level of GDP per capita is a driver only for high- and medium-income countries. Furthermore, we observe that rich highly vaccinated countries show a non-inclusive flow of vaccines towards less-vaccinated countries. Our results also highlight the heterogeneity according to the income of the countries.

Concerning the supply forces, we observe the importance of having an important pharmaceutical company in a country. This diminishes the flow of trade of human vaccines probably because part of the internal demand is satisfied by domestic production. At policy level, this result points out the importance of strategically promoting the production of human vaccines in medium- and low-income countries in order to decrease their dependence from richer countries. Furthermore, the export activity of human vaccines increases for countries with a strongly internationalised pharmaceutical industry. Although we did not explicitly control for favourable tax policies or for other specific trade regulations, we argue that they would likely have little impact on the production and distribution of highly complex products such as vaccines. Indeed, both phases require strict attention and high level of competences and capabilities (OECD, 2021; Yaqub, 2018) that shall be trained, before being able to attract companies with beneficial tax policies.

Finally, the challenges posed by COVID-19 are not solvable without correcting the growing disparities that have characterised the global human vaccine trade. Overcoming the pandemic and guaranteeing developing countries adequate tools to immunise their populations, will require a global strategy to accompany vaccine development. This needs to include, a stimulation of the manufacturing capacity in newcomer countries, and more favourable access to vaccines for poorer populations who are subject to a high disease burden. More generally, trade policies could be used in a more proactive way. This is even more valid when talking about health products, given their direct nexus with population health (Bhattacharjee & Chanda, 2023). Proposals such as the one contained in Ganslandt et al. (2001) date back to more than 20 years ago, but the recent global pandemic and the results of this paper shall contribute to the reactivation of this debate.

ACKNOWLEDGEMENTS

We thank the anonymous referees and the editor for their helpful comments and suggestions. We would like to thank Verònica Gombau for her research support, the participants to the XXIII Encuentros de Economía Aplicada and to the IIPPE 2022 conference in Bologna for constructive feedback.

FUNDING INFORMATION

This work was supported by Universitat Rovira i Virgili (2019PFR-URV-B2-80), the Consolidated Group of Research (2014-SGR-1395), and funding from the European Union's Horizon 2020 Research and Innovation Programme under the Marie Skłodowska-Curie grant agreement (No. 713679), from "GRINS – GROWING RESILIENT, INCLUSIVE AND SUSTAINABLE (cod. PE0000018) – CUP: H73C22000930001" and from the Universitat Rovira i Virgili (URV).

DATA AVAILABILITY STATEMENT

N/A.

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How to cite this article: Segarra-Blasco, A., Teruel, M., & Cattaruzzo, S. (2024). The international trade in human vaccines before COVID-19. *The World Economy*, *47*, 1978–2008. https://doi.org/10.1111/twec.13533

APPENDIX 1

TABLE A1 Market shares of the main exporters of human vaccines (periods 2000–2004 and 2015–2019).

	2000	2001	2002	2003	2004	2015	2016	2017	2018	2019	2000–2004	2015–2019
European Union	50.05%	49.42%	51.34%	50.55%	52.50%	46.29%	50.81%	51.23%	49.53%	47.67%	50.77%	49.10%
USA	18.01%	20.63%	23.81%	22.69%	15.70%	27.68%	21.82%	24.06%	25.19%	28.06%	20.17%	25.36%
United Kingdom	10.05%	8.38%	5.24%	7.04%	10.58%	7.99%	9.20%	9.46%	7.95%	6.63%	8.26%	8.25%
India	2.51%	1.13%	1.40%	1.93%	2.58%	0.95%	1.10%	0.96%	1.01%	1.14%	1.91%	1.03%
China	1.37%	1.06%	1.88%	1.35%	1.08%	0.84%	1.12%	1.60%	1.78%	3.82%	1.35%	1.83%
Russia	0.92%	1.50%	1.15%	0.99%	0.79%	0.48%	0.57%	0.49%	0.59%	0.39%	1.07%	0.50%
Switzerland	0.76%	1.27%	0.83%	0.95%	2.38%	0.25%	0.37%	0.49%	0.30%	0.41%	1.24%	0.37%
Singapore	0.17%	0.45%	0.14%	0.64%	0.10%	0.14%	0.17%	0.13%	0.17%	0.18%	0.30%	0.16%
Japan	0.13%	0.12%	0.10%	0.12%	0.15%	0.98%	1.55%	1.10%	1.05%	0.76%	0.12%	1.09%
Korea	0.02%	0.09%	0.03%	0.02%	0.09%	0.01%	0.01%	0.02%	0.02%	0.04%	0.05%	0.02%
Rest of Countries	16.00%	15.96%	14.10%	13.73%	14.05%	14.41%	13.29%	10.47%	12.42%	10.90%	14.77%	12.30%

Source: UN Comtrade.

TABLE A2 List of countries included in the analysis by cluster.

OECD	Middle-income countries	Low-income countries
Australia	Albania	Afghanistan
Austria	Argentina	Algeria
Belgium	Armenia	Angola
Canada	Azerbaijan	Bangladesh
Chile	Brazil	Bolivia
Colombia	Bulgaria	Cambodia
Czech Republic	China	Cameroon
Denmark	Costa Rica	Central African Republic
Estonia	Croatia	Congo
Finland	Cuba	Cote d'Ivoire
France	Cyprus	Egypt
Germany	Dominican Republic	El Salvador
Greece	Ecuador	Ethiopia
Hungary	Georgia	Ghana
Iceland	Guatemala	Guinea
Ireland	Hong Kong	Haiti
Israel	Indonesia	Honduras
Italy	Iran	India
Japan	Iraq	Kenya
South Korea	Jamaica	North Korea
Latvia	Jordan	Laos
Lithuania	Kazakhstan	Madagascar
Luxembourg	Kuwait	Mali
Mexico	Lebanon	Mauritania
Netherlands	Libya	Morocco
New Zealand	Malaysia	Mozambique
Norway	Malta	Nepal
Poland	Namibia	Nicaragua
Portugal	Oman	Niger
Slovak Republic	Panama	Nigeria
Slovenia	Peru	Pakistan
Spain	Romania	Paraguay
Sweden	Russian Federation	Philippines
Switzerland	Saudi Arabia	Rwanda
Turkey	Serbia	Senegal
United Kingdom	Singapore	Sudan
United States	South Africa	Syria
	Taiwan	Tunisia
	Thailand	Uganda

TABLE A2 (Continued)

OECD	Middle-income countries	Low-income countries
	United Arab Emirates	Ukraine
	Uruguay	Uzbekistan
	Venezuela	Vietnam
		Yemen
		Zambia
		Zimbabwe

Source: Own elaboration. Please note that for the classification of non-OECD countries according to the income groups, we referred to the World Bank classification.

TABLE A3 Description of variables.

Variable	Definition	Source
Dependent variables		
V	Export value of human vaccines	UN Comtrade
Control variables		
DIST	Distance between capital of both countries (in logs)	CEPII
COMMON	Dummy variable identifying if both countries share the same official language	CEPII
BORDER	Dummy variable identifying if both countries share the border	CEPII
FTA	Dummy variable which takes the value of 1 if both countries are in a free trade agreement	CEPII
Demand drivers		
POP_EXP POP_IMP	Population (in logs)	World Bank
GDPpc_EXP GDPpc_IMP	GDP per capita (in logs)	World Bank
MORE_VAX	Dummy tracking whether vaccines are flowing from countries with HIGH rates of full COVID-19 vaccinations (>70%) to countries with LOW rates (<40%; data updated: 15/10/2022). It is a binary and it takes the value of 1 if the previous condition holds	OWID
Supply drivers		
GL index	Variable that measures the existence of intra-industry trade in the market following Grubel and Lloyd (1975)	Own computation from UN Comtrade
PHARMA_PROD	Binary which takes the value of 1 if the in the pair of countries that compose the flow, the exporter has located a BIG PHARMA company in it while the importer does not. With BIG PHARMA, we mean pharmaceutical companies comparing in the TOP2500 R&D investor report	Own computation from JRC-Seville
PHARMA_EXP PHARMA_IMP	Share of pharmaceutical trade over total trade at country level (HS 3002) (in logs)	Own computation from UN Comtrade
SIMILAR	Absolute difference of the log GDP per capita between exporter and importer	Own computation from World Bank

TABLE A4 Descriptive statistics.

	Mean	Std. dev.	Min	Max
Export value	4,889,397	6.34E+07	0	4.24E+09
Population (exporter)	1.05E+08	2.61E+08	1,794,583	1.40E+09
Population (importer)	1.01E+08	2.57E+08	281,205	1.40E+09
Distance between countries	6171.41	4385.83	59.62	19,772.34
Common language (dummy)	0.165	0.371	0	1
Borders' contiguity (dummy)	0.062	0.242	0	1
GDP per capita (exporter)	22,495.70	21,159.11	111.93	102,913.50
GDP per capita (importer)	22,082.93	21,291.25	111.93	118,823.60
Similarity index	9.51	1.44	−0.004	11.64
Share of the pharmaceutical trade over total trade (exporter)	0.004	0.008	0	0.071
Share of the pharmaceutical trade over total trade (importer)	0.004	0.008	0	0.071
FTA (dummy)	0.327	0.469	0	1
More vaccinations (dummy)	0.081	0.273	0	1
Pharma producer (dummy)	0.337	0.473	0	1
GL index	0.040	0.148	0	1
Observations	58,947			

TABLE A5 Pairwise correlation matrix.

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
(1) Export value	1													
(2) Population (exporter)	0	1												
(3) Population (importer)	0.01*	−0.04*	1											
(4) Distance between countries	−0.04*	0.10*	0.10*	1										
(5) Common language (dummy)	0.04*	−0.01	0	−0.09*	1									
(6) Borders' contiguity (dummy)	0.06*	0.01	0.01	−0.30*	0.17*	1								
(7) GDP per capita (exporter)	0.09*	−0.19*	−0.10*	−0.03*	−0.07*	−0.06*	1							
(8) GDP per capita (importer)	0.05*	−0.10*	−0.18*	−0.03*	−0.06*	−0.05*	−0.05*	1						
(9) Similarity index	−0.02*	−0.19*	−0.18*	0.09*	−0.16*	−0.25*	0.33*	0.32*	1					
(10) Share of the pharmaceutical trade over total trade (exporter)	0.13*	−0.10*	−0.06*	−0.05*	−0.01*	−0.03*	0.63*	−0.06*	0.21*	1				
(11) Share of the pharmaceutical trade over total trade (importer)	0.04*	−0.05*	−0.10*	−0.04*	−0.02*	−0.03*	−0.07*	0.61*	0.20*	−0.06*	1			
(12) FTA (dummy)	0.03*	−0.13*	−0.13*	−0.53*	0.03*	0.28*	0.16*	0.16*	−0.01*	0.11*	0.10*	1		
(13) More vaccinations	−0.01*	−0.01	−0.08*	0.03*	0.04*	−0.07*	0.16*	−0.27*	0.12*	0.07*	−0.13*	−0.09*	1	
(14) Pharma producer (dummy)	−0.02*	0.21*	−0.18*	0.09*	−0.08*	−0.11*	0.50*	−0.42*	0.22*	0.31*	−0.27*	−0.07*	0.33*	1
(15) GL index	0.12*	0.01	0.01*	−0.16*	0.07*	0.16*	0.14*	0.14*	−0.06*	0.07*	0.07*	0.18*	−0.07*	−0.10*

***$p<.01$; **$p<.05$; *$p<.1$.

TABLE A6 Country leaders in intra-industrial trade of human vaccines. Gruebel and Lloyd index.

Country name	Mean	Standard deviation	Observations
Germany	0.370	0.313	538
Austria	0.347	0.312	292
Hungary	0.321	0.316	130
Italy	0.319	0.308	318
Denmark	0.316	0.293	276
Singapore	0.314	0.291	187
Czechia	0.314	0.321	154
Switzerland	0.291	0.289	326
Spain	0.287	0.271	272
Canada	0.282	0.307	248
United States of America	0.268	0.293	466
China	0.262	0.296	135
India	0.243	0.280	373
Australia	0.198	0.251	265
Ireland	0.240	0.291	180
Poland	0.196	0.287	153
United Kingdom	0.234	0.275	534
Netherlands	0.190	0.250	486
Japan	0.226	0.256	207
Belgium	0.184	0.265	581
Indonesia	0.181	0.248	124
Republic of Korea	0.156	0.229	245
No intra-industrial trade	0.000	0.000	50.505
Intra-industrial trade	0.256	0.2899	9.481

Note: N.B. The above table reports an extraction of the countries showing more intra-industrial trade for the whole period of observation, and with at least 50 intra-industrial transactions. Source: own elaboration.

APPENDIX 2

Analysis of the heterogeneity of the trade of human vaccines.

A relevant element in our analysis is the heterogeneity of the flows of trade in human vaccines. Accordingly, we disaggregate the total exports from a country into two different margins:

$$X_{i,t} = \sum_{n-1}^{N} X_{i,j,t} = N_{i,t} \times \overline{X}_{i,t}$$

where X_{ijt} is the volume of exports from country i to country j, $N_{i,t}$ is the number of countries where country i exports, and $\overline{X}_{i,t}$ represents the average export value that country i has in each destination country. Taking logs, we have the following equation:

$$ln\left(X_{i,t}\right) = ln\left(N_{i,t}\right) + ln\left(\overline{X}_{i,t}\right)$$

In a sense, we have split the total value of exports into an extensive margin (number of countries where the country is present) and an intensive margin (average value of exports).

Given the spatial distribution of the markets, we perform several analyses to check the skewness and kurtosis of our data. We expect that the UN Comtrade database will be highly skewed since a handful of countries accounts for most aggregate flows of human vaccines.

As expected, the correlation matrix in Table A7 shows a high correlation (0.9657) between intensive and total flows. Furthermore, there is a high correlation with the extensive margin (0.9077 and 0.7675 respectively).

Table A8 demonstrates that the skewness tests for the average export value show a non-significant p-value. The results for the kurtosis are, however, highly significant regardless of whether we consider the intensive margin or the number of markets. Hence, our results point to a small number of source countries acting as origins for a large number of final markets (Figure A1).

TABLE A7 Correlation matrix.

$ln(X_i)$	1		
$ln(\overline{X}_i)$	0.9657	1	
$ln(N_i)$	0.9077	0.7675	1

Note: All correlations are significant at 1% based on the Pearson correlation.

TABLE A8 Skewness/kurtosis tests for normality.

			From 2000 to 2008		From 2009 to 2019	
	Pr(skewness)	Pr(kurtosis)	Pr(skewness)	Pr(kurtosis)	Pr(skewness)	Pr(kurtosis)
$ln(\overline{X}_i)$	p-value = .34	p-value = .00	p-value = .98	p-value = .00	p-value = .71	p-value = .00
$ln(N_i)$	p-value = .00	p-value = .00	p-value = .00	p-value = .00	p-value = .32	p-value = .00

Source: Own elaboration.

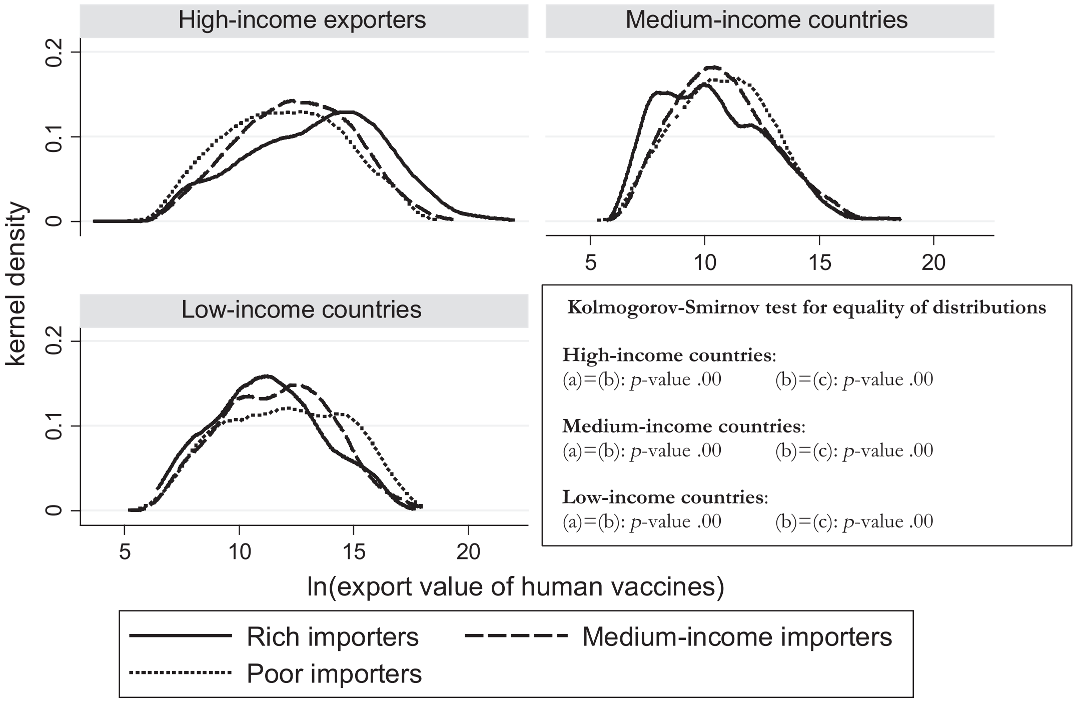

FIGURE A1 Export distribution (in logs) by income-country classification.