Covid-19 Vaccines, Innovation, and Intellectual Property Rights

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Abstract

Should the intellectual property rights on the first Covid-19 vaccines be temporarily lifted in applying the Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibility? Is it right to grant the first generation of Covid-19 vaccines a special treatment from an IPR perspective? On what grounds?

By extensively reviewing the available medical and economic literature on the subject, this chapter will guide the reader step by step to the leading scientific, political, and cultural challenges in granting broad worldwide access to vaccination.

The accumulated delays in providing effective Covid-19 vaccine intervention in the low- and middle-income countries are ultimately responsible for the virus circulation at the global level and the proliferation of immunity-escaping variants. Therefore governmental rationality around the world would suggest any possible active policy tool to scale up the current vaccines supply.

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However, not to prevent future investment in R&D, the governments should bear the cost of the expected increased industry obsolescence determined by a temporary patent waiver; this includes public patent buyouts and regulated public-private R&D partnerships.

"Many insisted that I patented the vaccine, but I didn't want to. It is my present to all the children of the world. [. . .] You see, they killed me two wonderful nieces, but I saved children from all over Europe." Albert Bruce Sabin, American-Polish medical researcher, developed the oral polio vaccine, President of the Weizmann Institute of Science in Israel 1969–1972. In this quotes he referred to Amy and Deborah, killed by the Nazis in Białystok, Poland.

Introduction

Because of the undergoing historical period, talking about the "economics of vaccines" immediately triggers an identification between vaccines and Covid-19 in the public's mind, as in most advanced economies, effective vaccination campaigns against the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) enormously impacted global public health and economic perspectives.

Spurred by this evidence, several contributions recently tried to capture the economic values of Covid-19 vaccines and specifically considered the interaction of different factors on the vaccination rollouts for a large set of countries. Determinant factors included the initial impact of the outbreak in terms of incidence of the disease, fatalities, and intensive care unit admissions during the early phases of the pandemic; supply-side factors such as early procurement of vaccine doses; and the domestic production of vaccines (see Deb et al. 2022, among others).

The vaccine industry is one of the most concentrated in the world. Until 2019, four firms – Pfizer, Sanofi, GKS, and Novartis – earned more than 80% of the world vaccine revenues. Yet, their vaccines mainly served the richest 20% of the world population, strenuously protecting their monopolistic rents with the patents and other intellectual property rights instruments. For example, the clinical trial results and other important documentation are held proprietary, which would render hardly effective a patent waiver. Such protection is not only crucial for vaccines, but for the many more other pharmaceutical products.

Unfortunately, the vaccine industry was considered one of the most vulnerable and least lucrative industries in the pharmaceutical sectors (Kremer and Snyder 2003). Since demand often comes from governments, the firms that have invested massively in the research and development (R&D) of new vaccines are always at risk of a hold-up problem, in case governments refuse to pay a fair price for their jabs. This is an important reason why vaccine producer firms often refuse to directly sell their jabs to middle-income and low-income countries. This usually leaves the majority of the world population uncovered by vaccines, at the mercy of pathologies that a European or a North American would never experience in their

life. Some producers offer vaccines to poor countries, most notably the Serum Institute of India (SII). SII is the world's largest vaccine producer in terms of quantity, but the prices of its jabs are so low that its total revenue is negligible compared to the patent holders of the rich world. Yes, SII does a much better service to India and several other countries than its most exclusive industry partners of the wealthy nations.

Covid-19 changed this scenario, because it massively increased the profitability of the vaccine industry. The combination of the pandemic severity and the huge macroeconomic costs of the non-pharmaceutical interventions (NPI) to contain the spread of the virus increased the demand for jabs to levels never imagined before. Billions of customers eager to vaccine themselves as soon as possible appeared, with governments strongly supporting them. Starting as a small biotechnological German firm, BioNTech sold $17 billion of its Covid-19 vaccine in 2021, with an estimated profits of at least half of it. BioNTech R&D costs in 2020, mainly devoted to its Covid vaccine, were $645 million. The German government supported its R&D with $445 million. This incredible scientific success is the result of several years of university and public research in the mRNA gene vaccines. Consequently, the research phase for the new vaccine was unexpectedly very fast: BioNTech received the genetic code of the new virus in January 2020, and its vaccine was ready for clinical trials by April 2020.

Pfizer was crucial in the clinical trial and approval stages, which attests on the division of R&D labor in this industry. Their vaccine was ready to use in the fall 2020. Pfizer/BioNTech set up a world record vaccine innovativeness and introduction speed, compared to the standard 4- to 10-year vaccine development time.

Pfizer is the real winner of this vaccine patent race, deserving at least the merit of being fast in identifying a promising German firm and in offering a deal to share the profits and appropriate the relevant patent. No European pharmaceutical firm showed comparable intelligence abilities, thereby relegating Germany to a mere customer of a German-made but US-appropriated patent on the first top-of-the-art Covid-19 vaccine.

Another formerly unknown rising star is Moderna, born a decade ago as a small biotechnological firm with a young and committed team firmly convinced of the potential importance of mRNA technology. This American firm managed to introduce its vaccine shortly after Pfizer, consolidating the United States' advantage in this vital industry for the world. Moderna too capitalized on more than three decades of basic research in mRNA and related technologies, which obtained – thanks to the Bayh-Dole Act – several university and public institutions patents eventually non-exclusively licensed to Moderna.

In a press conference of March 18, 2021, Ursula von der Leyen declared "We, Europeans, are excellent in making science with money. But we are not so good in making money out of science." Spurred by the continental Europe's lack of science-industry coordination attested by Pfizer's takeover of BioNTech mRNA vaccine, the European Commission set up the Health Emergency Preparedness and Response Authority (HERA), to monitor pandemic emergencies and potential new vaccine candidates, with the aim of timely mobilizing European pharmaceutical developers.

Quite frustrating for the European Union, post-Brexit United Kingdom ruled the world of the slightly less innovative but still highly effective and profitable vaccines, with its excellent science-industry coordination which allowed Oxford vaccine to get developed and commercialized by British AstraZeneca. Continental Europe, along with India's SII, became the main manufacturing hub of the British-patented Oxford/AZ vaccine.

Another very lucrative vaccine was developed and patented by Johnson and Johnson, which readily became popular because of its single-dose requirement.

China – with Sinopharm and Sinovac – and Russia, with Sputnik V, developed their vaccines. However, their effectiveness seems much lower, especially when facing the challenge of new virus variants. Consequently, as of March 2022, China still suffers a strict zero-Covid policy restricting international contacts and re-instating lockdowns. Russia still has a worryingly high virus mortality rate.

The Covid-19 pandemic vaccine high-income world market was dominated in 2020–2021 by the abovementioned four vaccines, with Pfizer being the only previous member of the pre-Covid vaccine quadrumvirate. The strict enforcement of vaccine patents was set to generously compensate the patent race winners of the Covid-19 pandemic, but raise the legitimate question of whether they left almost eight billion people at the mercy of a handful of profit-maximizing firms. This doubt is legitimate, because after a year and a half since production started, half of the world population remained unvaccinated, the virus kept mutating and reducing the efficacy of the vaccines, and the world economy lost massive production and trade possibilities due to the NPI interfering all over the place. Moreover, while richer countries have been treated as preferential customers, the big vaccine producers have mainly ignored the poorer potential customers such as those of the sub-Saharan Africa. India, after excruciating delays, managed to protect its population thanks to the unwavering effort of the SII.

More than 100 countries have asked WTO to temporarily waive Covid-related patents, to stimulate the entry of more firms worldwide and rump-up vaccine production. The wealthy countries blocked this proposal more times at the WTO. This reminded of the traditional poor-rich country opposition well-known in the pharmaceutical industry in the international political opposition to the application of the TRIPS, which led to the Doha Declaration (WTO 2003). Then something completely new happened: the new White House administration, with President Biden, joined the patent waiver proposal in May 2021. This pathbreaking White House position makes history in the IPR doctrine, as the most innovative world had never declared its availability to partly scarify IPR to help the world. The former European Parliament President David Sassoli echoed to "without taboos, to increase the production of vaccines." Eventually the European Union opted to oppose Biden's proposal at the WTO, leaving Covid-19 vaccine patents unsuspended.

Has the WTO strict enforcement of IPR slowed the worldwide vaccine Covid-19 production and herd immunity? Shall IPR be held responsible for new variants, like Omicron, to emerge in the unvaccinated part of the world? Would easier imitation have led to enough more production to immunize enough people in the world to

eliminate the Covid-19 virus from the planet? Is economics able to answer these questions vital for the world population and macroeconomy?

This chapter tries to summarize what economics can add to the relationship between IPR and vaccine in a serious pandemic such as Covid-19.

The structure of this chapter is as follows: First, section "The Global Market for Vaccines" reviews the central economic and medical literature on vaccines before the Covid-19 pandemic. Second, section "The Covid-19 Vaccine Case from a World Perspective" analyzes the different scientific rationales that the available literature has so far proposed in support of a broader Covid-19 mass global-scale vaccine immunization campaign. Further to that, section "The Case for a Covid-19 Patent Waiver" derives the conditions that should be desirable from a social perspective to guarantee Covid-19 vaccines a differential treatment also from the point of view of IPR policy. In particular, section "The Case for a Covid-19 Patent Waiver" outlines a stylized model to instruct policy on the desirability of temporarily suspending vaccine patents. Depending on the crucial parameters of the model, it may or may not be desirable to waive vaccine patents temporarily. The user-friendly policy rule can readily provide estimates of the extra vaccine R&D public funding needed to compensate innovators of the future patent suspensions. Finally, section "Summary" wraps up the conclusions.

The Global Market for Vaccines

Before extending the analysis to the Covid-19 case, it is here useful to highlight the stylized facts of the economics of vaccines, which are obviously shared characteristics of the Covid-19 vaccine industry.

The first relevant stylized fact is that state authorities regulate the vaccine market highly. An extensive health economics literature highlighted the reasons for the traditional state interventionism in the vaccine industry. These reasons are mainly because the individual's private incentive to vaccinate may substantially differ from the public (state's) incentive to vaccinate from a social perspective. See Annemans et al. (2021) and Costa-Font et al. (2021), among others.

Vaccines that are efficacious against infection have aggregate health impact by reducing the burden of disease through direct protection of those vaccinated and reducing transmission, thus providing indirect protection to the population. This positive externality of individual vaccination on several other people's infections is not accounted for by the individual, who at most cares about his or her strict relatives. Hence, compared with most other available healthcare interventions, vaccines offer particular benefits in many ways. However, cohort asymmetries affect the incidence of a given disease and the severity of the disease, complications, and long-term consequences. Unlike other medical technologies, vaccines are preventive. This simple consideration pins down private (non-state) demand for vaccines significantly when a specific cohort is asymmetrically affected by the disease. On the one hand, this calls for state intervention to correct this suboptimal tendency of the decentralized vaccine markets. However, in the absence of

coercive interventions, the effectiveness of a vaccination campaign also requires broad societal support to reach herd immunity. See Betsch et al. (2013), Blanchard-Rohner et al. (2021), and Dewatripont (2021), among others.

From a development perspective, large-scale vaccination campaigns (e.g., rotavirus) showed that, when vaccines are made broadly available to the population, LICs are prone to support vaccine interventions effectively. This renders the so-called anti-vax social attitude a middle- and high-income countries' feature. The public health value of vaccination depends on whether other treatments are available to reduce morbidity and mortality. Among the lowest spectrum of global income levels, the overall levels of health services and therapeutic options are so poor that, given the incidence of the pathogen on the population, mortality and long-term public health negative consequences of not vaccinating are much higher for LICs than for HICs, with a corresponding paradox for the vaccine becoming very cost-effective in LICs, but relatively less in low-middle- to high-middle-income countries (Annemans et al. 2021; and Hogan et al. 2021).

It is worthwhile to recall here the historical milestone achievements of vaccination in the fight against human life-endangering infectious diseases: the global eradication of smallpox (1980); the eradication of polio at the worldwide level, i.e., the reduction of polio cases by 99.5% at the worldwide level (since 1988, thanks to the oral vaccine developed and unpatented by Albert Sabin); the first vaccine based on recombinant technology (1986); the first polysaccharide-protein conjugate vaccine (1987); the application of adolescent vaccines (HPV 2009); and, finally, the approval of the first two mRNA vaccines by the end of 2020.

Estimates show that actually vaccines prevent more than 20 currently life-threatening infective diseases, saving about 2–three million deaths every year (Lobo 2021). Although an overwhelming evidence shows that vaccines are among the most cost-effective of all public health technologies, in general, the standard public frameworks for the economic evaluation of public health programs tend to reflect more the private incentive for vaccination, which undervalues the full range of health and economic benefits conferred by vaccines. Hence, the health economics literature duly developed a rich normative analytical framework to assess the monetary value of vaccines. This literature is also motivated by the fact that current national vaccination strategies would imply a structural underestimation of the economic benefits of vaccines compared to other pharmaceutical products (see Postma and Standaert 2013).

Once individuated the causes of such underestimation, better-informed policymakers should opt for greater international cooperation and standardization of the procedures supporting global mass vaccination campaigns. The set of proposed useful analytical tools included introducing appropriate discounting techniques to estimate the long-term benefits of the vaccination programs and introducing fairness considerations, which are able to heavily affect the attractiveness of a vaccination program, like in case of the CIA's fake vaccination campaign organized in support of the captures of Osama Bin Laden (see Martinez-Bravo and Stegmann 2021). See also Bos et al. (2004), Beutels et al. (2008a, b), and Westra et al. (2012).

In general, lack of international coordination and poor standardization of vaccination programs are considered among the leading causes of inadequate cost-effectiveness of vaccine interventions, as has been shown by several studies on the decentralized introduction of rotavirus vaccination in neighboring European countries (the Netherlands, Belgium, the United Kingdom, and France). See Jit and Edmunds (2007); Standaert et al. (2008); Bilcke and Beutels (2009); Bilcke, Van Damme, and Beutels (2009); and Rozenbaum et al. (2011).

Although vaccines are medicinal products centrally approved by international health regulatory authorities (the WHO checks and monitors the effectiveness and safety requirements of new vaccines), each country acts independently when it comes to market access. Market access and reimbursement procedures of medicinal products are diverse across states. National health budgets often distinguish between vaccines that are part of children's basic vaccination programs (e.g., diphtheria-tetanus-pertussis vaccine, rotavirus vaccine), from vaccines that are part of dossier-specific reimbursement tracks (e.g., influenza vaccines), just like any other medical product.

As for August 20, 2020, in sub-Saharan Africa, 15 large epidemic outbreaks, other than Covid-19, were recorded. They are summarized by Tables 1 and 2.

Tables 1 and 2 present a list of 41 SSA countries, visually arranged from A (Angola) to L (Liberia) in Table 1 and from M (Malawi) to Z (Zimbabwe) in Table 3, respectively. For each country, table shows the data about the presence in the country of recent non-Covid-19 (*NC*) large epidemic episodes (second column) and the Covid-19 incidence (*C* – third column). Countries marked with the suffix $*NC$ are considered affected principally by non-Covid-19 epidemics, while countries marked with the suffix $*C$ are considered at high Covid-19 incidence, but they are not significantly affected by non-Covid-19 epidemic diseases. Finally, countries marked with the suffix $**$ (i.e., Ethiopia, Ghana, Ivory Coast, Kenya, Nigeria, Sudan, and Zambia) are badly performing with regard to both perspectives, as they show both the presence of non-Covid-19 large epidemic episodes and a high Covid-19 incidence.

Table 3 lists the non-Covid-19 epidemic diseases present in SSA according to Coker et al. (2021), which are considered rare disease and for which no available prophylactic vaccine or therapy exists.

A disproportionately large burden of these infective diseases hits the 0–19 sub-Saharan Africa (SSA) population, including measles, type 2 polio, and yellow fever (Coker et al. 2021). In SSA, anyway, the fraction of population belonging to ages 0–14, which are considered among the highest virus spreaders, is significantly higher than in the rest of the world (fifth column), ranging from an average of 41.26% in Eastern and Southern Africa to an average of 43.12% in Western and Central Africa, against a world average of 25.48% (WDI 2021).

By looking at these data, the full extent of the pervasiveness of industry well-documented market failures dramatically emerges. In fact, as for type 2 polio, Lassa fever, leishmaniasis, Crimean-Congo hemorrhagic fever, and Chikungunya, they are considered rare diseases at the world level, as they only affect developing countries which contribute to a small part of the world population (Table 3). Consequently,

Table 1 Epidemic Outbreaks by Country

Country	Large non-Covid-19 outbreaks	Covid-19 incidence	Total population	Population ages 0–14% of total population	Population % of world population
*NC Angola	Measles, vaccine-resistant Polio (type 2)	1000 < 4999	32,866,268	46.40	0.42
*NC Benin	Vaccine-resistant Polio (type 2), Lassa fever	1000 < 4999	12,123,198	41.94	0.16
*NC Burkina Faso	Vaccine-resistant Polio (type 2)	<1000	20,903,278	44.37	0.27
*NC Burundi	Cholera, Measles	1000 < 4999	11,890,781	45.25	0.15
*NC Cameroon	Measles, vaccine-resistant Polio (type 2)	<1000	26,545,864	42.06	0.34
*NC Central African Republic	Measles, vaccine-resistant Polio (type 2)	1000 < 4999	4,829,764	43.54	0.06
*NC Chad	Measles, vaccine-resistant Polio (type 2)	<1000	16,425,859	46.49	0.21
*NC Democratic Republic of Congo	Cholera, Ebola, Measles, Monkeypox, Plague, vaccine-resistant Polio (type 2)	5000 < 14,999	89,561,404	45.80	1.15
Eritrea	Unreported	<1000	6081	23.98	0.0001
** Ethiopia	Cholera, Measles, vaccine-resistant Polio (type 2)	15,000–29,999	114,963,583	39.92	1.48
Gabon	Unreported	5000 < 14,999	2,225,728	37.26	0.03
Gambia	Unreported	1000 < 4999	2,416,664	43.95	0.03
** Ghana	Vaccine-resistant Polio (type 2)	>30,000	31,072,945	37.13	0.40
*NC Guinea	Measles, Lassa fever vaccine-resistant Polio (type 2)	5000 < 14,999	13,132,792	43.05	0.17
** Ivory Coast	Vaccine-resistant Polio (type 2)	15,000–29,999	26,378,275	41.51	0.34
** Kenya	Cholera, Measles, Leishmaniasis	15,000–29,999	53,771,300	38.59	0.69
Lesotho	Unreported	<1000	2,142,252	32.24	0.03
*NC Liberia	Measles, Lassa fever	1000 < 4999	5,057,677	40.37	0.07

Table 2 Epidemic Outbreaks by Country

Country	Large non-Covid-19 outbreaks	Covid-19 incidence	Total population	Population ages 0–14% of total population	Population % of world population
Malawi	Unreported	1000 < 4999	19,129,955	42.99	0.25
*NC Mali	Measles, Yellow fever	1000 < 4999	20,250,834	47.01	0.26
*NC Mauritania	Crimean-Congo hemorrhagic fever, Dengue fever	<1000	4,649,660	39.69	0.06
*NC Mozambique	Cholera, Measles	1000 < 4999	31,255,435	44.06	0.40
*NC Namibia	Hepatitis E	1000 < 4999	2,540,916	36.84	0.03
*NC Niger	Measles	1000 < 4999	24,206,636	49.67	0.31
** Nigeria	Cholera, Yellow fever, Measles, Lassa fever, vaccine-resistant Polio (type 2)	>30,000	206,139,587	43.49	2.66
*C Republic of Djibouti	Unreported	15,000–29,999	988,002	28.91	0.01
Guinea	Unreported	1000 < 4999	13,132,792	43.05	0.17
*NC Republic of Congo-Brazzaville	Chikungunya	1000 < 4999	5,518,092	41.27	0.07
Rwanda	Unreported	1000 < 4999	12,952,209	39.47	0.17
*C Senegal	Unreported	15,000–29,999	16,743,930	42.59	0.22
Sierra Leone	Unreported	1000 < 4999	7,976,985	40.34	0.10
*NC Somalia	Chikungunya, Cholera	1000 < 4999	15,893,219	46.15	0.20
*C South Africa	Unreported	>30,000	59,308,690	28.80	0.76
*NC South-Sudan	Chikungunya, Measles	1000 < 4999	11,193,729	41.33	0.14
** Sudan	Chikungunya, Dengue fever, Diphtheria	15,000–29,999	43,849,269	39.80	0.56

(continued)

Table 2 (continued)

Country	Large non-Covid-19 outbreaks	Covid-19 incidence	Total population	Population ages 0–14% of total population	Population % of world population
Tanzania	Unreported	<1000	59,734,213	43.55	0.77
Togo	Unreported	1000 < 4999	8,278,737	40.64	0.11
*NC Uganda	Cholera	1000 < 4999	12,952,209	39.47	0.17
*NC Union of the Comoros	Dengue fever	1000 < 4999	869,595	39.02	0.01
**Zambia	Vaccine-resistant Polio (type 2)	15,000–29,999	18,383,956	44.02	0.24
*NC Zimbawe	Anthrax	1000 < 4999	14, 862,927	41.91	0.19

Table 3 Epidemic Outbreaks by Country

Country affected by epidemics as on May 2020	Population % of world population
Chikungunya	
Republic of Congo Brazzaville	0.07
Somalia	0.20
South Sudan	0.14
Sudan	0.56
Total SSA susceptible pop. % of world pop.	0.99
Lassa fever	
Nigeria	2.66
Benin	0.16
Guinea	0.17
Liberia	0.07
Total SSA susceptible pop. % of world pop.	3.05
Crimean-Congo hemorrhagic fever	
Mauritania	0.06
Total SSA susceptible pop. % of world pop.	0.06
Leishmaniasis	
Kenya	0.69
Total SSA susceptible pop. % of world pop.	0.69
Type-2 Polio	
Angola	0.42
Benin	0.16
Burkina Faso	0.27
Cameroon	0.34
Central Africa Rep.	0.06
Chad	0.21
Congo, Dem. Rep.	1.15
Ethiopia	1.48
Ghana	0.40
Guinea	0.17
Ivory Coast	0.34
Nigeria	2.66
Zambia	0.24
Total SSA susceptible pop. % of world pop.	7.90

they are practically ignored by the R&D efforts of profit-oriented pharmaceutical multinational companies (MNCs), as they are not considered a profitable investment, at the point that, at the moment, no approved prophylactic vaccine is available for such diseases.

For example, in SSA, Chikungunya epidemics are considered active in four countries (Republic of Congo Brazzaville, Somalia, South Sudan, and Sudan), resulting in 0.99% of the world population. Anyway, in 2007 a first Chikungunya outbreak (250 cases, of which 1 mortal) hit a HIC, Italy, followed by a second acute

episode (500 infections, with no mortality), always in Italy, in 2017. Similarly, SSA markets for potential prophylactic vaccines for Lassa fever, leishmaniasis, and the Crimean-Congo hemorrhagic fever constitute only 3.05%, 0.69%, and 0.06% world population, respectively. However, as regards type 2 polio, quite worryingly from a global public health perspective, it is active in 13 SSA countries, together amounting to the 7.90% of global population (see Table 3).

Also, for this reason, the current public debate shows great interest in the possibility that public research institutions actively engage in vaccine development and production to cover the many documented cases where the private sector lacks the adequate motivation to produce vital medical products. Anyway, the impact of legislative innovations like the Bayh-Dole Act has generated diffused concern about moving intellectual property protection upstream to basic innovators (see Cozzi and Galli 2017, 2021).

The Covid-19 Vaccine Case from a World Perspective

The impact of the Covid-19 world pandemic on the global economy has been unprecedented in modern nonwar times. The immense negative macroeconomic impact drove governments to implement effective vaccination strategies in the shortest possible time laps.

From a global Covid-19 perspective, particularly worrying appear to be the cases of Nigeria, with less than 5% of the population vaccinated as of March 2022, and Ethiopia, also with less than 5% of the population vaccinated as of March 2022, which separately account for the 2.66% and 1.48%, respectively, of the world population (see Coker et al. 2021).

In SSA anyway, the fraction of population belonging to ages 0–14, which are considered among the highest virus spreaders, is significantly higher than in the rest of the world: it ranges from 41.26% in Eastern and Southern Africa to an average of 43.12% in Western and Central Africa, against a world average of 25.48% (WDI 2021). Most infective diseases hitting harder on the young population also cause potentially severe impediments to human capital accumulation. This hits especially in LICs, where infections targeting more formative, younger ages can result in widespread cognitive underdevelopment, lower school attendance, worse educational attainment outcomes, and less attractive employment prospects as adults. Connolly et al. (2012) and Kotsopoulos et al. (2015) considered the long-term beneficial fiscal consequences of protecting the youth population from disease by appropriate vaccination, in the case of the rotavirus infection and the human papillomavirus (HPV) infection, respectively.

However, since from February 2020 up to October 2020, there were no vaccinations nor proven prophylactic medicines against SARS-CoV-2, nor proven treatments for recovery from Covid-19, the non-pharmaceutical (NP) methods of epidemiological control largely adopted included school closures as a public health policy routine, with resulting negative consequences in terms of human capital accumulation also in the HICs (see Agostinelli et al. 2022; Chetty et al. 2020;

McBryde et al. 2020; Karatayev et al. 2020; Brooks-Pollock et al. 2020; and Head et al. 2020).

Back in 2005, Smith, Yago, Millar, and Coast (2005) proposed to collect and estimate all economic consequences of infective disease episodes (including changes in supply and consumption behaviors, the effects on taxation, and the altered use of labor and capital), within a computable general equilibrium model to assess the costs of international public health emergencies, though recent contributions highlighted the empirical difficulty in estimating the whole magnitude of the macroeconomic effects of the recent severe acute respiratory syndrome (SARS) outbreaks. See Beutels et al. (2003), Beutels et al. ((2008a, b), Beutels et al. (2009), Smith et al. (2009), Keogh-Brown and Smith (2008), Keogh-Brown et al. (2010), and Prager et al. (2017).

The most recent utilitarian welfare with Covid-19-induced-mortality macroeconomic approach interpreted the Covid-19 economic shock as a reduction in the productivity of the quarantined individuals. Hence, these models usefully captured the aggregate utility loss from intertemporal infection increases (without vaccines) and the related increased severity of the NP interventions. Anyway, in this setting, aggregating individual well-beings with cohort asymmetry with respect to the pathogen is far from straightforward from a normative point of view. See Acemoglu, Chernozhukov, Werning, and Whinston (2021); Jones, Philippon, and Venkateswaran (2021); Boucekkine, Caravajal, Chakraborty, and Goenka (2021a); and Boucekkine, Chakraborty, and Goenka (2021b) among others.

Here, this chapter systematically reviews the health and economic modeling literature on Covid-19 vaccination, academically or independently developed to serve public health policymakers in their efforts to minimize Covid-19-related mortality, transmission, and morbidity outcomes. In addition, they support governments worldwide to achieve shared vaccination goals at the global and national levels.

To the extent that in the real world, what is perceived as urgent does not necessarily reflect what is essential, and this is particularly often true concerning public health policies, at the current global fight against Covid-19, the big elephant in the room is to ensure decent vaccination coverages for LICs. In fact, according to the World Health Organization (WHO), an inclusive global access to Covid-19 vaccines, along that suggested by COVAX vaccine-sharing initiative, is also the optimal strategy to reduce the potential global mortality from variants (viral strains hosting genetic mutations that increase transmissibility, change immune response, or affect the disease severity).

Moreover, to correctly frame the theme, one should note that at least for three main reasons, the Covid-19 vaccine's case is a special case within the economic literature on vaccines, particularly from an innovation-based scholar's perspective. First, from a production point of view, innovative mRNA vaccines result from a change in the technological paradigm of vaccine production. This change massively draws upon public investment in basic research in advanced leading research countries. After combining ex ante public funding and guaranteed government pre-orders, about $5.75 billion for Moderna and $2.5 billion for Pfizer/BioNTech.

The mRNA technology is particularly appreciated because it provides the highest coverage against contracting SAR-Cov-2 and because the manufacturing of the intermediate components of mRNA vaccines is less complicated than the "traditional" (cell-based, non-mRNA) vaccines. Indeed, the mRNA molecules are far more straightforward than proteins and the human body artificial viral proteins themselves, which are the intermediates in the traditional technologies (Lobo 2021).

For this reason, mRNA vaccine manufacturing can take place in much smaller bioreactors (e.g., 30–50 liters) than those generally adopted for traditional vaccine production (e.g., 2000 liters), according to Wen, Ellis, and Pujar (2015) and Park and Baker (2021). The production facilities (installed capital and equipment) can be an order of magnitude smaller, and, as a consequence, the financing costs for vaccine producers are lower. Most importantly when considering the welfare increases deriving from raising the actual supply capacity, because of the small-implant-scale nature, setting up production processes and covering investment expenses is cheaper for mRNA vaccines; and the production process can be quickly retargeted for new variants or even for new viral threats (see Pardi et al. 2018). BioNTech reconverted a cancer biological manufacturing facility into a Covid-19 vaccine manufacturing facility, with staff retraining, in 6 months.

From an innovation perspective, mRNA vaccines could be considered patented basic research. In fact, their potential application goes far beyond Covid-19 vaccines, as they constitute an almost general cost-saving production technology, viable of utilization for a broad set of different vaccines (Pardi et al. 2018, among others). Since Green and Scotchmer (1995), various theoretical and empirical approaches to sequential innovation in economics warned public regulators against the possibility that blocking patents could emerge in strategic basic R&D sectors, with the effect of restricting access to basic research sectors hampering future research avenues (Aghion and Howitt 1996; Schotchmer 2004; Chu et al. 2012; Cozzi and Galli 2014). Hence, mRNA technologies are an outbreak in basic scientific research, which should be adequately rewarded, but with a careful eye on the possible emergence of wicked incentives from an aggregate innovation perspective. See also Kiedaisch (2015); Gersbach, Sorger, and Amon (2018b); Heinemann (2019); and Akcigit et al. (2021).

Hence, understanding that mRNA vaccine manufacturing happens on a smaller scale and it is cheaper and faster to establish compared to non-mRNA technologies is the crucial first step to analyze the impact of policies both from the perspective of the innovators' incentives and from the point of view of the aggregate welfare gains deriving from the same innovations. See Kis et al. (2020a) and Kis et al. (2020b).

Secondly, the unprecedented global economic crisis generated by the Covid-19 world pandemic put considerable pressure on both vaccine producers and intergovernmental health organizations to guarantee Covid-19 vaccination to the world population in the shortest time lapse. Never before modern national health systems had to deal with such a globalized public health challenge. Trade interdependencies with unvaccinated countries impose a sizable economic drag on the vaccinated countries (Çakmaklı et al. 2021).

Finally, the public health value of vaccination depends on the population's risk profile, among other things. Hence, based on purely demographic considerations, the expected beneficial impact of Covid-19 vaccination is most significant in high-income countries (HICs) since these have the largest elderly populations and, therefore, the highest propensity to pay the public costs of mass vaccination campaigns.

This observation renders the field of Covid-19 vaccines particularly exposed to age-bias considerations at the national and international levels. If from a technological perspective, Covid-19 vaccines are considered a change in the paradigm of vaccine production (in particular the most innovative mRNA vaccines); from a global demand perspective, the requests of Covid-19 vaccines are distorted in favor of HICs, who are also those countries who can afford to pay more. Unlike retrovirus vaccines, whose introduction effectively increased children's life expectancy in sub-Saharan Africa thanks to GAVI Alliance, Covid-19 vaccines are freely provided within the national health systems of HICs. This is in line with the general observation that welfare states of HICs are considerably more age-oriented than those of LICs. Therefore, assessing the economic impact of the Covid-19 vaccines in HICs should take into account that aggregate productivity also includes quantifiable nonmarket productivity gains attributable to unpaid activities often performed by the elderly population, such as volunteering or philanthropic work and caregiving for children, grandchildren, or sick people.

In the global strategy against Covid-19, the focus of biomedical scientists and virologists has been reaching herd immunity by vaccination early enough. Most notably, before that, the global circulation of the new coronavirus implied that the SARS-CoV-2 wild strain changes in such unpredictable ways, meaning the re-exposure of those previously infected or vaccinated individuals. See Caldwell et al. (2021) for a recent extensive survey of the available research material on epidemiological mathematical modeling of Covid-19 herd immunity, with vaccines and different virus variants scenarios.

To quantify the level of population immunity (e.g., vaccine coverage) needed to achieve herd protection, epidemiological modelers calculate the herd immunity threshold (*HIT*). The *HIT* is a helpful tool to guide vaccination campaigns, which, in its simplest expression, assumes homogeneous mixing (i.e., assumes that contact rates among all individuals in the population are uniformly distributed) and implies the following well-known formula:

$$HIT = 1 - \frac{1}{R_0},$$

where R_0 denotes the average number of secondary infections from each infectious individual in a fully (or partially) susceptible population. In other words, "R_0 is the basic reproduction number, or the average number of susceptible individuals that are infected by a single infected individual" (Agarwal and Reed 2021).

In practice, *HIT* varies by context, as contacts and infections do not distribute uniformly within populations based on individual and aggregate factors like age,

behaviors, contact patterns, physical distancing, naturally achieved immunity, and vaccine coverage. Hence, for Covid-19, the focus should be on attaining substantial levels of herd protection to slow down the spreading of the disease. Early Covid-19 studied estimated a *HIT* of 60–70% based on initial R_0 estimates of 2.5–3.5 (Wu et al. 2020; Musa et al. 2020; and Alimohamadi et al. 2020). However, the first SARS-CoV-2 Alpha variant has been estimated to be 60% more transmissible than the wild-type SARS-CoV-2 strain, implying a HIT of 80% (Davis et al. 2021).

Agarwal and Reed (2021) slightly extend the previous model to refine its empirical results. Knowing, as of time t, the values of the infection basic reproduction parameter R_{0t}, a given population fraction of infected, a given reinfection rate f_t for infected, and vaccine effectiveness E_t, Agarwal and Reed (2021) show that the minimum amount of vaccinated population fraction guaranteeing herd immunity, $vaccinated_t^*$, is obtained with this formula:

$$vaccinated_t^* = \frac{1 - \frac{1}{R_{0t}} - (1 - f_t)Infected_t}{E_t}$$

Unlike in Agarwal and Reed (2021), all parameters change over time. For example, vaccine efficacy in a population can drop after 6 months from the last vaccine, etc. Base immunity is $B_t = Infected_t + Vaccinated_t$. Hence the effective reproduction number is $R_t = (1 - B_t)R_{0t}$. Herd immunity is obtained when $R_t = 1$.

Calibrating parameters realistically, they find that a vaccination threshold $vaccinated_t^* = 45 - 60\%$.

Much of future global pandemic scenarios will depend on how the viral strains evolve according to natural selection. Caldwell et al. (2021), among others, note that, in general, viruses become more transmissible and less pathogenic over time. They often evolve into endemic diseases, and similar mutations can arise in different world regions, given the exposure to worldwide similar natural selective pressures.

As this process of natural selection leads to multiple co-circulating variants, with varying transmissibility, severity, and responsiveness to pharmaceutical interventions, alternative aggregate epidemiological outcomes are susceptible to prevail. In particular, when co-circulating strains provide cross-immunity (i.e., infection from either variant confers high levels of immunity to both strains), disease models show that:

1. Viral competition favors variants with higher R_0, leading to *strain replacement* (Keeling and Rohani 2008).
2. When strains display similar R_0 values, *epidemic cycles* are likely to emerge, which mimic seasonal influenza epidemic cycles (Gupta et al. 1998; Gomes et al. 2002; Keeling and Rohani 2008).

Fitting mathematical models with the time series of strain infection incidence (in the context of SARS-Cov-2, this means the incidence of the variances so far identified, from Alpha to Omicron) allows epidemiologists to estimate strain-specific growth rates, R_0, and the extent of cross-immunity conferred to other strains (Davies

et al. 2021). Basically, achieving significant levels of global herd protection implies shifting the focus on keeping the global cross-strain average infection rate R_t below one, allowing to achieve both low levels of sustained viral transmission (causing endemic cycles) and acute epidemic episodes contained in their absolute magnitude.

Using a disease model that considers long-term immunity and homogeneous mixing in the *HIT*, Caldwell et al. (2021) showed that herd immunity can become unattainable with co-circulating viral strains with increased transmissibility and/or immune evasion. For example, a vaccine that is 90% effective at reducing a strain-specific infection transmission (e.g., Moderna against the SARS-Cov-2 wild-type strain) would require at least 62% vaccine coverage to achieve herd immunity; but if vaccine-escaped viral mutants lead to a vaccine efficacy less than 60% (the authors provide evidence that this is the actual tendency of SARS-Cov-2 ongoing natural evolution), diffused herd immunity cannot be achieved through vaccination alone.

According to this realistic scenario, to prevent regular or periodical hospital congestions, with still relatively high death tolls over the following years, countries will hamper the transmission of SARS-Cov-2 variants among the population by regular vaccine booster doses (like for the seasonal influenza viral strain). Also, likely will be new socially and economically painful NP epidemiological control methods (i.e., broad restrictions to people's liberties, lockdowns, sectorial business shutdowns, school closures, etc.) to buffer the most acute phases of the epidemic due to the increased R_t. See Goenka and Liu (2013 and 2020); Goenka, Liu, and Nguyen (2014, 2021); and Goenka (2021).

Allocating available vaccine doses in proportion to each country's population size (compared to the current practices favoring HICs) is close to the optimal strategy (Hogan et al. 2021) and could double the global number of deaths averted (Chinazzi et al. 2020):

> "If high-income countries can preferentially obtain a large proportion of the available vaccine doses at the expense of lower income countries then we would expect an additional 900 deaths per million from this less efficient global allocation." Hogan et al. (2021)

Of the about 1.6 billion vaccine doses administered to date, only 0.3% was destined to the poorest countries. The current state of allocations of Covid-19 vaccine doses to the LICs has been described as worrying and requiring immediate action from governments of both developing and developed countries, as the Covid-19 pandemic will not be over unless it is assured that vaccines are made available everywhere (Gurwitz 2021).

As amply discussed, the vaccines sector is considered one of the most vulnerable and probably the least lucrative industries in the pharmaceutical sectors (see Kremer and Snyder 2003). Here, pervasive market failures prevent the industry from satisfying the effective demand, thereby triggering periodic shortages of products which are vital for public health and economic development: historically, vaccines supply shortages have been more the rule than the exception (see Lobo 2021, among others).

A few large producers dominate the global vaccine production, consistently with significant scale economies and noncompetitive behaviors. Large ex ante investments in both R&D and specialized physical capital and equipment are required to install a critical productive capacity. Consequently, it is rational for operating vaccine producers to try to smooth the utilization of the installed productive capacity over the medium-long run and postpone reaching herd immunity in the HICs. The latter are market segments primarily targeted by pharmaceutical MNCs' price-setting strategy. Just as Adam Smith noted in his 1776's classics, it would indeed not be judged as wise, someone who expects their dinner from the benevolence of the butcher, the brewer, or the baker (Smith 1776).

Given the global aggregate shortage of vaccines, prioritizing Covid-19 vaccination within and between countries has been a source of public health concerns and an ethical challenge for international policymakers. Forslide and Herzing (2021) focused on characterizing the inter-temporal trade-off between reaching herd immunity and the price-setting behavior of an influenza-type vaccine's monopolistic producer. But, in a closely related epidemiological paper, Hogan et al. (2021) analyze a global epidemiological model with different vaccination scenarios for different age groups to best assess the intra-country age profile and the global allocation of Covid-19 vaccine doses. Like Forslide and Herzing (2021), during the first stages of the pandemic, if the target is to reduce mortality, HICs should prioritize covering their old-age individuals. During a more mature phase of a successful vaccination campaign, anyway, provided that the target is to eradicate SARS-CoV-2, younger individuals, who are the highest spreaders, should be given priority; and vaccine doses should be allocated proportionally to population also to LICs. Current COVAX plans favor a global allocation strategy that prioritizes the highest-risk groups – including the elderly – and suggest an "equitable" vaccine allocation strategy. Each country receives doses in proportion to its population size and epidemic status.

According to Forslide and Herzing (2021), the middle-aged should have priority if economic productivity is the main target. In fact, vaccines enhance labor force productivity in many ways. In particular, because vaccines can prevent diseases and their resulting disabilities, they contribute to aggregate productivity by lowering absenteeism at work, which not only leads to lost production output but also increased unemployment expenses for the social welfare system. See also Bärnighausen et al. (2014), Bilcke et al. (2014), and Annemans et al. (2021).

Recently, the empirical study of Deb et al. (2022) used cross-sectional variation in vaccination rates to assess the expected impact of the virus varying into more transmissible strains (with a higher R_0), on a large set of countries. Consistently with the prediction of Caldwell et al. (2021), their results suggest that from a medium-term perspective, as long as the vaccine distribution is unequal across countries, no country is safe, even those achieving high vaccination outcomes. The rapid spread of the Delta variant from India to neighboring countries is considered the paradigmatic case of cross-border spillovers from protracted epidemic waves: the Delta variant became the dominant coronavirus in Asian countries and in North America over a 1–3-month period after becoming the dominant variant in India.

However, the central novelty of Deb et al. (2022) consists in constructing daily proxies of "foreign" Covid-19 cases and vaccines in neighboring countries, based on geographic proximity and realistic trade linkages. New Covid-19 cases in neighboring countries contribute to an increase in a country's own infections, but on the positive side, there are considerable positive spillovers from increased vaccinations in neighboring countries. Such spillovers are compelling motivation for international cooperation to scale vaccine production at the global level and to ensure adequate distribution of vaccines to all countries, including by sharing excess doses (Lamy 2020).

In a related study, Çakmaklı et al. (2021) also focus on international trade, production linkages, and unequal vaccine allocations. This study estimates that the global economic costs due to missing to vaccinate 50% of the LICs' population might be as high as $3.8 trillion. Hence, making the vaccine globally available ". . . is not an act of charity, but an act of economic rationality for the advanced economies to get involved in the efforts for an equitable global vaccine distribution" (Çakmaklı et al. 2021, p. 3).

A country's epidemic circulation not only impacts its production and employment as a pure domestic supply shock, but it also impacts the production of intermediate inputs imported by other countries. To capture these international value-chains spillovers, Çakmaklı et al. (2021) incorporated the global intersectoral input-output linkages into a susceptible-infected-recovered (SIR) epidemiological model. This approach allowed them to quantify the cascading effect of sectorial supply shocks in different countries via global value chains and international production linkages. When vaccination is complete, sectorial demand and supply shocks get immediately reabsorbed in vaccinated countries. As a consequence, the economic costs of the pandemic due to negative domestic sectorial demand and supply shocks disappear in vaccinated countries; however, the costs arising from the international trade network persist as long as foreign countries are not vaccinated.

The Case for a Covid-19 Patent Waiver

This section analyzes whether it should be desirable (or not) from a global social perspective to guarantee Covid-19 vaccines a differential treatment also from the point of view of IPR policy.

"Intellectual property" is a notion referring to several different legal instruments: patents, trademarks, copyrights, designs, and undisclosed information are some examples of IPR provided for under the TRIPS Agreement (see Watal 2001, among others.) Patents and undisclosed information are forms of intellectual property closely relevant to vaccines. For example, patents (Articles 27–38 TRIPS) protect inventions. In contrast, a broad class of undisclosed information (Article 39 TRIPS) potentially includes both information relating to vaccine production processes and aspects of vaccine clinical trial or other relevant test data.

Recently, different global political stakeholders (including the European Parliament and the US President Joe Biden) demanded the temporary lifting of IPR

protection for Covid-19 vaccines, to address vaccine production bottlenecks and hence to accelerate the global vaccine rollout. In his statement of Nov. 26, 2021 about the Omicron variant, the US President Joe Biden said:

> I call on the nations [. . .] to meet the U.S.challenge to waive intellectual property protections for Covid vaccines, so these vaccines can be manufactured globally. I endorsed this position in April; this news today reiterates the importance of moving on this quickly.

On October 2, 2020, the Indian and South African governments presented a formal proposal for a patent waiver, following specific provisions of the agreements on TRIPS. See WTO (2020). The waiver would prevent the current patent holders of Covid-19 vaccines from blocking vaccine production elsewhere on the grounds of patents and allow countries to produce Covid-19 medical products locally or import or export them more easily. More than 100 of the 164 WTO member states declared themselves in favor of India and South Africa's proposal for a temporary waiver of patents on Covid-19 vaccines as part of the agreements on TRIPS. Still, after intense bilateral and multilateral talks on this issue, the consensus required by the WTO has not been reached.

In fact, all recent Covid-19 patent waiver proposals encountered a numerically limited, but still influential opposition, from a part of the international IPR policy experts' community (aligned with the arguments of vaccines' producers), which ultimately raised the point that the potential detrimental effect of a patent waiver on future innovation's incentives may overcome the beneficial effects of an effective global-wide Covid-19 vaccination coverage. In particular, they suggested that by reducing the return on investment in R&D, the temporary patent waiver would permanently dismantle the same IPR system that provided the products needed to put the pandemic to an end, penalize pharmaceuticals, stifle biomedical innovation, and finally deter future investments in R&D. Thambisetty et al. (2021) point out the need to accompany mandatory IPR measures on Covid-19 vaccines with other incentives to pharmaceutical MNCs to share knowledge. In particular, they argue that without sufficient active engagement by the pharmaceutical industry (the current owners of IPR, data and know-how to address the pandemic), mandatory mechanisms like a patent waiver or compulsory licenses could result extremely complex and time-consuming to implement in additional vaccine production. See also Gurry (2020)'s considerations of the non-IPR barriers to access to vaccines a therapeutical product against Covid-19.

The argument was advanced, among others, that traditionally IPR did not significantly impact the price-setting strategies of vaccine manufacturers, for example, in the case of the recombinant DNA hepatitis B vaccines, where the maximum patent license royalty rate was 15%. However, it appears that the recombinant DNA hepatitis B vaccine experienced effective price competition from a plasma-derived hepatitis B vaccine, independently provided by two South Korean manufacturers (the Cheil Sugar Company and the Korean Green Cross Corp.).

Interestingly, Cuba developed two homemade Covid-19 vaccines: Abdala and Soberana 02, both ideally given in three doses. By the end of 2021, the country

immunized more than 90% of its population, and it started exporting the Cuban Covid-19 vaccines to partner countries, conditional to the WHO approval. According to the evolution of the epidemics, Cuba saw a big spike in the SARS-CoV-2 infection cases in August 2021 – when Cuba's vaccine coverage was still relatively low – but new infections in the country have since then continuously declined and remained low. Although without further empirical investigation, it is difficult to gauge how much of this success is to be due to the vaccines, the virus' suppression coinciding with the country reaching high vaccine coverage is a positive sign. See Reardon (2021), Toledo-Romani et al. (2021), Chang-Monteagudo et al. (2021), Head (2021), and Taylor (2021). Currently, Vietnam and Venezuela have received Abdala doses, while both Abdala and Soberana 02 doses have been sent to Iran for clinical trials. Nicaragua has given emergency authorization to both Cuban vaccines; Mexico and Argentina declared themselves interested in using these vaccines.

A crucial step will be the expected WHO approval, and after that, new data will be released which will allow the experts to evaluate the efficacy of the Cuban Covid-19 vaccines. Until then, and probably also afterward to some extent at least, it is good academic practice to take the concerns related to the effective productive capacity of the outsider competitors very seriously. In fact, potential challenges with scaling up mRNA vaccine production include the limited availability of industrial specific know-hows and skilled human capital, which are both essential to implement the new technology, along with quickly sourcing raw materials (e.g., the cationic lipid) in the required quantities.

The problem is exacerbated anyway by the fact that patented vaccines have their fundamental components and background technologies patented as well, which complicates, even more, the outsiders' ability to imitate the final technology (see Namboodiri 2020, among others). Also, for this reason, it is strategic for LICs to build universal medical productive capacities and welfare systems, to share knowledge and technologies, and to prioritize the production and the distribution of a broad set of home-made pharmaceutical inputs, medicines, and vaccines, along the model pursued by Cuba, which anyway was forced into developing medical and sanitarian autarchy by trade restrictions. See Augustin (2022), Head (2021), and Meredith (2022), among others.

To try to overcome the problem of multi-patented technologies used in the final Covid-19 vaccines, the approval of a Covid-19 Technology Access Pool (C-TAP) was proposed during early stages of the pandemic (see de Menez 2021). Ideally, C-TAP should have been working as a voluntary licensing scheme for "existing and future rights in patented inventions and designs, as well as rights in regulatory test data, know-how, cell lines, copyrights and blueprints for manufacturing diagnostic tests, devices, drugs, or vaccines" related to Covid-19 (Munoz Tellez 2021). In fact, the global R&D system and the business model of pharmaceutical companies are based on the enforcement of their IPR over drugs and other knowledge-based assets, but, as Suzanne Schotchmer noted back in 2004, the legal rights conferred by patents economically corresponds to a veto power over the manufacturing of a patented technology (see Scotchemer 2004). As a consequence,

the international community has a political due to first look after "cooperative" solutions together with the pharmaceutical MNCs, before considering moving toward more drastic and controversial measures, like a temporal patent waiver or compulsory licensing. See Thambisetty et al. (2021).

Although initially the C-TAP proposal was received with great enthusiasm, over time optimism has diminished due to the low commitment of developed countries and lack of interest from the pharmaceutical MNCs (de Menez 2021). For this reason, the WHO launched the Access to Covid-19 Tools Accelerator (ACT): a global collaboration program designed to accelerate development, production, and equitable access to Covid-19 tests, treatments, and vaccines (Lamy 2020). The ACT Accelerator is structured on four pillars: diagnostics, treatment, vaccines, and health system strengthening. The vaccine procurement pool (COVAX) is the vaccines pillar; the Coalition for Epidemic Preparedness Innovations (CEPI) coordinates vaccine development and manufacturing; the WHO oversees policy and allocation issues, and the GAVI, The Vaccine Alliance is responsible for procurement and delivery of vaccine doses. Essentially, COVAX is a pool for procurement and equitable distribution of vaccines: by aggregating the demands of different countries and supporting different suppliers, it is meant to reduce the purchase prices and avoid the natural risks of developing and producing vaccines, as too global supply shortages.

In the recent past, bulk purchasing and procurement processes proved very successful in reducing the price of the hepatitis B vaccine (see Garrison 2004), and further alternative mechanisms have been proposed to facilitate access to patented vaccines including tiered pricing finally the recourse to compulsory licensing.

Tiered pricing is a traditional mechanism for facilitating access to vaccines. This is in part because parallel importation tends not to take place given the "cold chain" nature of vaccine distribution. However the phenomenon of schedule divergence, where different vaccine products are now provided to segments of markets that used to share a single vaccine product, may threaten the use of tiered pricing.

Nowadays, compulsory licenses related explicitly to medicines are possible in most national legislation. A specific compulsory license on a patented technology can be granted where the patent holder has abused his monopoly or where it is otherwise in the public interest. Whether or not the necessary know-how is possessed by a potential compulsory licensee will impact the effectiveness of compulsory licensing, as too the effectiveness of patent waiving. However, the practical value of mandatory license provisions in the patent law is that of a powerful deterrent. Usually, the threat induces the grant of contractual licenses on reasonable terms. Thus the aim of actually manufacturing the patented invention is accomplished. Anyway, a notable precedent in the vaccine industry is the compulsory license granted in Israel in 1995 for the manufacturing of the DNA hepatitis B vaccine covered by a Biogen patent (Cohn 1997). In Australia, in at least two cases, the Trade Practices Act of 1974 was applied concerning incumbent monopolists' refusals to deal (O'Bryan 1992); and two applications for compulsory licenses were reported in South Africa in 1993 (Sheppard 1994).

Like any voluntary mechanism to increase R&D cooperation, C-TAP and COVAX's success depend on the participation and direct collaboration of pharmaceutical MNCs, the sole legal owners of the patented technologies. At the end of April 2021, Covax shipped only one fifth of its projected estimates vaccine doses (see Erfani et al. 2021), and pharmaceutical MNCs have made no formal commitment to broad voluntary licensing schemes (de Menez 2021). In this sense, the current TRIPS patent waiver framework seems to be at the moment the political and institutional response with the most significant potential to guarantee the scaling of the production of vaccines developed to fight Covid-19.

A Model to Assess a Covid-19 Patent Waiver

Cozzi (2022) focused on the following points covered by the recent debate on Covid-19 vaccine patent waiver:

1. A low probability of more firms producing Covid-19 vaccines in the case of a patent waiver.
2. A high expectation of a future patent waiver.
3. Government spending in R&D subsidy to keep R&D working.

Cozzi (2022) incorporated the previous points to draw conclusions about the desirability of a patent waiver. Paradoxically, it turns out that these three critical points raised against patent waivers turn out to be powerful arguments in favor of it.

While a patent suspension will increase future firm entry, it will also dissuade current R&D.

The mathematical outcome depends on the following three numbers:

1. The probability of new firms producing the vaccine if the government suspends the patent: p.
2. How many vaccine doses would the new entrant firms produce relative to monopolistic patent holder production: Q_E/Q_{NE}, where Q_{NE} is jabs production in case of no entry, and $Q_E > Q_{NE} > 0$ the jabs produced in case of competitive entry.
3. How much would the patent holder profits drop after competitive entry: V_{NE}/V_E, where V_E is the patent holder's profit in case of entry, and $V_{NE} > V_E \geq 0$ be its profit in case of no entry.

The Cozzi (2022) shows that an expected patent waiver will increase the expected available vaccines if and only if the following inequality holds:

$$p\left(\frac{Q_E}{Q_{NE}} - 1\right) + 1 > \frac{1}{p\left(\frac{V_E}{V_{NE}} - 1\right) + 1}. \tag{1}$$

Under condition $\frac{Q_E}{Q_{NE}} > 2 - \frac{V_E}{V_{NE}}$, inequality (1) is equivalent to the following condition for the probability that after a waiver competitive firms will successfully enter the patented vaccine industry:

$$p \in \left(0, \frac{\left(\frac{Q_E}{Q_{NE}} - 1\right) + \left(\frac{V_E}{V_{NE}} - 1\right)}{-\left(\frac{V_E}{V_{NE}} - 1\right)\left(\frac{Q_E}{Q_{NE}} - 1\right)}\right] \tag{2}$$

Therefore, the probability of imitators succeeding in copying the vaccine know-how cannot be high for the patent waiver to be beneficial.

In the case of Covid-19, it is widely believed that mRNA vaccines are very difficult to imitate because of the highly specialized know-how needed for their manufacturing. Interestingly, if this is true, the patent waiver will likely improve the expected future mRNA vaccines availability.

For example, assuming $Q_E = 2Q_{NE}$ and $V_E = 0.5V_{NE}$, then (1) becomes

$$p(2-1) + 1 > \frac{1}{p(0.5-1) + 1}.$$

that is,

$$0.5\,(1-p)p > 0$$

which is satisfied for all $p < 1$.

Cozzi (2022) permits an evaluation of how much more R&D subsidies will be needed for the government to neutralize the disincentive effects of another expected waiver on the R&D for new vaccines. If the pre-waiver R&D subsidy rate is denoted s, after the waiver it will have to increase to

$$s^* = s_{NE} + \frac{V_{NE} - V_E}{V_{NE}} p(1 - s_{NE}). \tag{3}$$

With $p = 0.10$ and $V_E = 0.5V_{NE}$, the increase in the subsidy rate needed to neutralize the patent waiver would be less 5%.

Hence, if the technological gap between the HICs' manufacturers, i.e., the technological incumbents and the LICs' outsiders, is high, gving LICs a chance to catch up by imitation with HICs' technology (by temporarily waiving the IPR) would not significantly affect the industry expected technological obsolescence. Therefore, with a small public subsidy paid to the vaccine developers proportionally to the R&D cost, the governments would re-optimize innovators' incentives in the next period. With a relatively small fiscal correction, governments could restore the intertemporal incentives to innovation provided by the IPR enforcement. Otherwise, the estimated benchmark global economic cost due to missing to vaccinate 50% of LICs' population is as high as $3.8 trillion, of which 49% to pay by the same advanced economies through global value-chain cascade effects (Çakmaklı et al. 2021).

Summary

Vaccines play a crucial role in improving global public health, with the ability to stem the spread of infectious diseases and the potential to eradicate them. However, the Covid-19 pandemic, with its enormous human and financial costs, suddenly reminded us of the precariousness of the human condition for the possible pathogenic events that nature can generate by itself.

The international epidemiological and economic, scientific community, along with international organizations and governments of developed and developing countries, repeatedly stated worries about the availability of Covid-19 vaccine doses in sufficient quantity and at affordable prices for the most vulnerable and marginalized populations in the world.

Several mutated SARS-CoV-2 viruses have already emerged, and variants can better evade vaccine-induced immune responses. Moreover, worldwide infection numbers have been climbing since February 2021 and coming in waves; by April 2021, case trajectories were growing exponentially in some places. Accordingly, lockdowns and NP interventions returned to be an option in several nations around the globe; and still, Covid-19 is on its way to becoming endemic.

Due to variants and waning immunity, specific vaccine boosters may be needed annually or every 6 months. In March 2022, China has started a strict lockdown in its Jilin province, despite nearly 90% of its population being vaccinated. The needed additional boosters could be on the order of 5 or 10 billion vaccinations a year, or over 10 or 20 billion doses for two-dose vaccines, to be equitably and effectively distributed all over the world. Unless governments guarantee the scaling of the global vaccine production to allow timely, sufficient, and affordable access to all preventive technologies developed against Covid-19, SARS-CoV-2 is likely to continue circulating and evolving around the globe as an endemic disease (i.e., with epidemic cycles), possibly with medium-sized acute epidemic episodes (Goenka et al. 2021).

Although the existing viral strains arose separately, they have commonalities represented by changes in specific sites of the spike protein, likely because of similar selective pressures, e.g., increasing immunity (Caldwell et al. 2021). Through natural evolution, SARS-CoV-2 will likely continue spreading and shift to primary infection among younger age groups (Lavine et al. 2021; Caldwell et al. 2021), with possible devastating long-term consequences for the economies of the developing countries due to demographic reasons (see Tables 1 and 2; Musa et al. 2020; and Coker et al. 2021). And for the world economy as a whole (Çakmaklı et al. 2021).

The international scientific community amply supported the proposal of a temporary patent waiver for Covid-19 vaccines as a tool to increase global supply, achieve global herd immunity, and advance global health equity. However, without vaccine manufacturing liberalization, there will not be jabs fast enough to prevent the spread of SARS-Cov2 variants, the avoidable deaths, and the continuing choking of low- and middle-income countries through poor health (Erfani et al. 2021, among others), with enormous consequences also for the advanced economies.

At the same time, innovation must be globally rewarded. Although sometimes hardly criticized (see Kremer and Williams 2010; Pagano and Rossi 2009; Belloc and Pagano 2013; Boldrin and Levine 2013, among others), the global implementation of a modern IPR system happened during the middle 1990s, when many developing countries joined the WTO. The TRIPS provided the right legal instrument and appropriate economic incentive to support innovation and technological development worldwide, by allowing mainly middle-income economies to shift from imitation-intensive production regimes into knowledge-intensive productions – characterized by domestic innovation with well-designed and adequately enforced IPR laws (see Banerjee and Nayak 2014, among others). Since then, the predominant mode of private R&D incentivization has been throughout IPR and the TRIPS Agreement. The monopoly power granted by globally enforced patents earned innovative MNCs sufficient profit to repay R&D. At the same time, the bulk of basic research in HICs keeps being financed or directly carried out by public sector institutions, which traditionally pair with private R&D firms to develop their scientific knowledge into viable products (see Akcigit et al. 2021, among others).

This chapter showed that the governments can take an active role in supporting private R&D on new and better vaccines, while at the same time promoting the know-how transfer needed to guarantee a production booster and reach world herd immunity. Therefore, overcoming knowledge transfer impediments, including those operating via IPRs, will be crucial to defeat the Covid-19 pandemics. The insights of this chapter will be also helpful for other pandemics.

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