

# COVID-19 Vaccines: What Are the Global Health Consequences of a Third Dose?

Series | COVID-19 and response strategy

**ISGlobal** Barcelona  
Institute for  
Global Health

**Authors:** Clara Marín, Adelaida Sarukhan and Marta Rodó (ISGlobal)\*

This document is partially based on [Statement on the third dose of COVID-19 vaccines \(16/09/2021\)](#) by the Multidisciplinary Collaborative Group for the Scientific Monitoring of COVID-19.

[ This document is a one of a series of discussion notes addressing fundamental questions about the COVID-19 crisis and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light. ]

8 October 2021

Photo: Mat Napo / Unsplash

Late 2020 saw the start of the largest vaccination campaign ever undertaken—an effort hailed as the beginning of the end of the SARS-CoV-2 pandemic. It was hoped that global health governance mechanisms would allow for a relatively equitable distribution of vaccines among countries, but the reality has turned out to be quite different. At present, **vaccine coverage is dangerously unequal**. The full vaccination rate in the European Union stands at 62.9%. Spain is one of the most advanced countries in this regard, with 77.4% of its population having received a full vaccine regimen. Meanwhile, in many low- and middle-income countries, rates of full vaccination remain trivial: 0.4% in Niger, 0.3% in South Sudan, 0.2% in Turkmenistan.<sup>1</sup>

This disproportion poses a major **ethical problem**, puts the **health of the entire planet** at risk and requires **global action**

so that the pandemic response can be managed fairly and efficiently.

Amid this dilemma about the unequal distribution of vaccines, most countries with high vaccination rates have embarked on a new debate about the need for a third dose. However, in order to develop rational, effective and fair vaccination plans, we must answer some **key questions**: **Who** should receive a third dose? Does a third dose **make sense** for the general population? **Is it ethical** to administer third doses at a time when a majority of the population in many countries has yet to receive the initial regimen? Is an extra dose **essential** to control the pandemic? ●

\* Clara Marín is a medical resident in Preventive Medicine and Public Health at Barcelona's Hospital Clinic and a regular collaborator with ISGlobal's Department of Policy and Global Development. Adelaida Sarukhan is an immunologist and scientific writer at ISGlobal. Marta Rodó is a junior analyst at ISGlobal.

With the collaboration of Gonzalo Fanjul, Policy Director at ISGlobal, and Rafael Vilasanjuan, Policy and Global Development Director at ISGlobal.

<sup>1</sup> Covid-19 vaccine tracker: the global race to vaccinate. *Financial Times*.

# 1. What Does the Scientific Evidence Say?

**“The amount of antibodies in the blood decreases after vaccination, but the evidence suggests that, although prevention of infection and symptomatic disease does decrease, protection against serious consequences such as hospitalisation or death remains strong.”**

A growing body of research shows that both natural immunity and vaccine-induced immunity to SARS-CoV-2 are robust and, in both cases, the immunological memory is likely to last for several years.<sup>2</sup> **The vaccine has been shown to be highly effective** at preventing death and severe disease, despite the passage of time. Several laboratory studies point to the diminished capacity of serum from vaccinated individuals to neutralise some of the variants of concern circulating today. However, all COVID-19 vaccines currently approved in the United States and Europe remain highly effective at protecting against hospitalisation, ICU admission and death, regardless of variant.

It is true that the amount of antibodies in the blood decreases over time after vaccination, and evidence shows that a booster dose increases the titres of these antibodies to the levels found immediately after the second dose.<sup>3</sup> What is not clear is whether these decreases reflect a decrease in protection against the virus. The evidence suggests that **prevention of infection and symptomatic disease does decrease**, while **protection against serious consequences** such as hospitalisation or death remains strong.<sup>4,5</sup>

Given that the evidence shows that a full vaccination regimen is sufficient to protect against severe disease and death, we can conclude that a third dose is not necessary for the general population, although there are **high-risk groups for whom a third dose could be beneficial**. The first such group is **immunocompromised people**, for whom the evidence recommends a third dose as part of the primary vaccination regimen, rather than

as a booster dose. A booster dose may be appropriate for **especially vulnerable groups**, such as **older adults** or **institutionalised people**, or for those who are continuously exposed to the virus, such as **health care workers**. In **Spain**, this is currently the strategy: a third dose for some groups of immunocompromised patients<sup>6</sup> and a plan to administer a booster dose to those over 65 years of age.<sup>7</sup>

The **European Medicines Agency (EMA)** recently issued a statement endorsing a third dose for immunocompromised people. The EMA also supports the consideration of a possible third dose for the general population, although it specifies that there is no direct evidence that a booster dose increases protection against the virus and advises that close attention be paid to the emerging evidence.<sup>8</sup> Thus, the EMA has opened the door to the possibility of massive administration of third doses under the **precautionary principle**, as this measure could have short-term benefits in vaccinated populations that are at low risk of adverse effects.

However, these recommendations do not **incorporate a global health vision**. Introducing a third dose for populations that are already vaccinated will always be associated with **exceptional localised benefits**. However, these benefits must be viewed in the context of a **global battle against the virus** in which no one is safe until everyone is safe. The **most effective strategy** for controlling the pandemic and dealing with new viral variants is to increase vaccine coverage globally, rather than providing booster shots to the vaccinated population, with the exceptions noted above ●

<sup>2</sup> Juliá Blanco, Adelaida Sarukhan, Quique Bassat, Magda Campins, Robert Guerri, Carles Brotons, Juana Díez, Mireia Sans, Josep M Miró y Silvia de Sanjosé. [Statement on the third dose of COVID-19 vaccines \(16/09/2021\)](#). *ISGlobal*. September 2021.

<sup>3</sup> Ewen Callaway. [COVID vaccine boosters: the most important questions](#). *Nature*. August 2021.

<sup>4</sup> AlQahtani, M.; Bhattacharyya, S.; Alawadi, A.; Mahmeed, H. Al; Sayed, J. Al; Justman, J.; El-Sadr, W.M.; Hidary, J.; Mukherjee, S. [Morbidity and mortality from COVID-19 post-vaccination breakthrough infections in association with vaccines and the emergence of variants in Bahrain](#). *Research Square*. 2021, doi:10.21203/rs.3.rs-828021/v1.

<sup>5</sup> Chemaitelly, H.; Tang, P.; Hasan, M.R.; Coyle, P.; Ayoub, H.H.; Kanaani, Z. Al; Shaik, R.M.; Rahim, H.F.A.; Gheyath, K. [Waning of BNT162b2 vaccine protection against SARS-CoV-2 infection in Qatar](#). *MedRxiv*. 2021.

<sup>6</sup> Pablo Linde. [Unos 100.000 pacientes inmunodeprimidos empezarán ya a recibir la tercera dosis de la vacuna contra la covid](#). *El País*. 7 September 2021.

<sup>7</sup> Sanidad administrará una tercera dosis de la vacuna a los mayores de 70 años. *El País*. 5 October 2021.

<sup>8</sup> Comirnaty and Spikevax: EMA recommendations on extra doses and boosters. *European Medicines Agency*. 4 October 2021.

# 2. The Global Health Perspective

**“No one is safe unless everyone is safe. This statement is more than just an attractive slogan; it reflects the reality of a pandemic caused by a highly contagious disease in a globalised world.”**

Most countries with high vaccination rates that have initiated a booster-dose campaign have done so only for vulnerable groups. However, a few countries have rolled out **third-dose mass vaccination campaigns**. The most prominent example is **Israel**, which is offering a booster dose to every vaccinated person over 12 years of age.<sup>9</sup> Israeli authorities have reported a decrease in severe morbidity, although it has not been demonstrated that this is due to the third dose. The **United States** has announced that it will also provide a booster dose to all adults who request one.<sup>10</sup>

To further complicate matters, many countries are stockpiling vaccines that they end up not using, because of either poor planning or over-ordering,<sup>11</sup> to the point that **many doses expire** and cannot be used.

The international community has tried to **correct this imbalance**, with questionable success. The **COVAX initiative**—coordinated by Gavi, the Vaccine Alliance, the Coalition for Epidemic Preparedness Innovation (CEPI) and the World Health Organisation (WHO)—was created early in the pandemic with the goal of providing equitable access to COVID-19 vaccines in resource-poor countries.<sup>12</sup> COVAX pledged to ensure that at least 20% of the population in all countries would be immunised by the end of 2021.

The **reality** is that the vaccines have not reached most of the world. Vaccine nationalism has caused the vast majority of doses to become concentrated in the richest countries, which are better able to negotiate with pharmaceutical companies. Meanwhile, countries with fewer resources have been left to their own bilateral negotiating

capacity or to alarmingly poorly endowed cooperation mechanisms.

This situation has given rise to other alternatives for vaccine acquisition, such as the **African Vaccine Acquisition Task Team**, organised by the African Union, which has managed to acquire 400 million doses for the continent.<sup>13</sup> The relative failure of North-South solidarity strategies and the self-absorption of richer countries has led to a **sense of abandonment** among resource-poor nations and a return to colonialist models of cooperation.

In addition to this enormous ethical conflict, the fact that vaccination rates in many countries are negligible poses a **risk to everyone**, creating pockets of populations susceptible to contagion, viral transmission and the emergence of new variants. Evidence shows that equitable vaccine distribution has enormous benefits: it reduces the burden of disease in resource-poor countries, reduces the cost of surveillance of imported cases and minimises the evolution of the virus.<sup>14</sup> Indeed, the slogan of COVAX is “**No one is safe unless everyone is safe.**”<sup>15</sup> This statement is more than just an attractive slogan; it reflects the reality of a pandemic caused by a highly contagious disease in a globalised world.

In the short term, there is an **urgent need for global mass distribution of vaccine doses**, either through **existing mechanisms** or through **bilateral donations** (see *Box 1* for more information about the limitations of this model). In the longer term, the solution necessarily requires a **comprehensive global health strategy** based on sound governance that reconciles ethical, practical and scientific considera-

<sup>9</sup> Ari Rabinovitch. [Israel offers COVID-19 booster to all vaccinated people](#). *Reuters*. 29 August 2021.

<sup>10</sup> Zaria Gorvett. [Covid-19: How effective is a third vaccine dose?](#) *BBC*. 16 September 2021.

<sup>11</sup> Pablo Linde. [La gestión de las vacunas contra la covid en tiempos de abundancia: el reto ahora es evitar que caduquen](#). *El País*. 24 September 2021.

<sup>12</sup> [COVAX explained. Gavi, the Vaccine Alliance](#). Gavi, the Vaccine Alliance. 3 September 2021.

<sup>13</sup> Sarah Wheaton, Ashleigh Furlong. [The globe's new public health strategy: Every country for itself](#). *Politico*. 9 September 2021.

<sup>14</sup> Wagner, CE.; Saad-Roy, CM.; Morris, SE.; Baker, RE.; Mina, MJ.; Farrar, J.; Holmes, EC.; Pybus, OG.; Graham, AL.; Emanuel, EJ.; Levin, SA.; Metcalf, CJE.; Grenfell, BT. [Vaccine nationalism and the dynamics and control of SARS-CoV-2](#). *Science*. 2021 Sep 24;373(6562):eabj7364. doi: 10.1126/science.abj7364. Epub 2021 Sep 24. PMID: 34404735.

<sup>15</sup> [COVAX: Working for global equitable access to COVID-19 vaccines](#). World Health Organisation (WHO).

tions. Immunisation strategies in all countries should be designed with the global as well as the national context in mind. It is also important to **ensure the transfer of knowledge and technology** so that vaccines can be developed and manufactured in low- and middle-income countries,<sup>16,17</sup>

with the aim of boosting the immunity independence of these states and achieving more effective management of the pandemic ●

**Table 1. Countries with highest and lowest rates of full vaccination.**

Countries with the highest rates of full vaccination	%	Countries with the lowest rates of full vaccination	%
Portugal	84,1	Democratic Republic of the Congo	0,04
United Arab Emirates	83,7	Yemen	0,2
Malta	81,8	Turkmenistan	0,2
Singapore	79,7	Benin	0,2
Spain	77,4	Chad	0,2
Iceland	75,5	Central African Republic	0,2
Denmark	75	South Sudan	0,3
Chile	74,1	Cameroon	0,3
Uruguay	74	Guinea-Bissau	0,4
Ireland	73,8	Niger	0,4

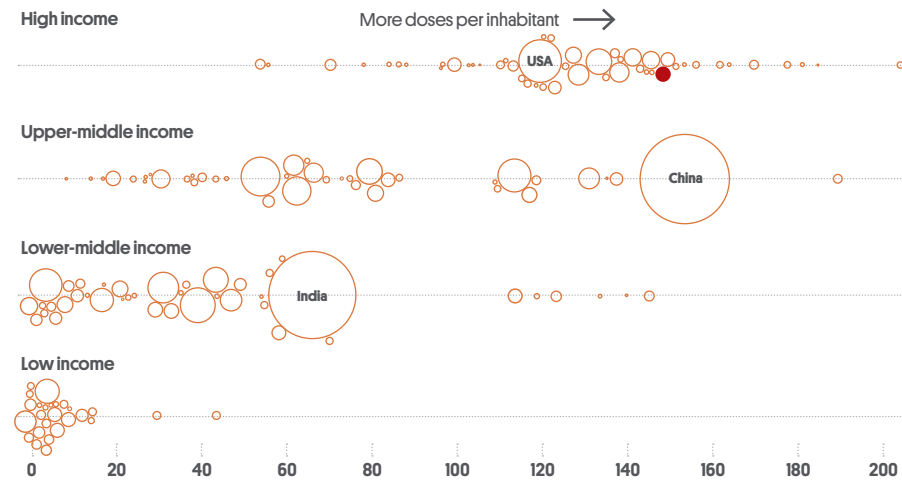
Source: [Covid-19 vaccine tracker: the global race to vaccinate](#). *Financial Times*.

<sup>16</sup> Tara Haelle. [Can This Houston-Born COVID Vaccine Save the Developing World?](#) *Texas Monthly*. 16 July 2021.

<sup>17</sup> Pitisuttithum, P.; Luvira, V.; Lawpoolsri, S.; Muangnoicharoen, S.; Kamolratanakul, S.; Sivakorn, C.; Narakorn, P.; Surichan, S.; Prangpratanporn, S.; Puksuriwong, S.; Lamola, S.; Mercer, LD.; Raghunandan, R.; Sun, W.; Liu, Y.; Carreño, JM.; Scharf, R.; Phumratanaprapin, W.; Amanat, F.; Gagnon, L.; Hsieh, CL.; Kaweeponroj, R.; Khan, S.; Lal, M.; McCroskery, S.; McLellan, J.; Mena, I.; Meseck, M.; Phonrat, B.; Sabmee, Y.; Singchareon, R.; Slamanig, S.; Suthepakul, N.; Tcheou, J.; Thantamnu, N.; Theerasurakarn, S.; Tran, S.; Vilasmongkolchai, T.; White, JA.; Garcia-Sastre, A.; Palese, P.; Krammer, F.; Poopitapol, K.; Wirachwong, P.; Hjorth, R.; Innis, BL. [Safety and Immunogenicity of an Inactivated Recombinant Newcastle Disease Virus Vaccine Expressing SARS-CoV-2 Spike: Interim Results of a Randomised, Placebo-Controlled, Phase 1/2 Trial](#). *medRxiv* [Preprint]. 2021 Sep 22:2021.09.17.21263758. doi: 10.1101/2021.09.17.21263758. PMID: 34580673; PMCID: PMC8475960.

### Figure 1. Vaccination gap among countries by income level.

Number of doses administered per 100 inhabitants in each country, grouped by income level. The size of the bubble indicates the population of the country. Vaccination in Spain highlighted.



**Source:** Ana Ordaz, Victòria Olivares and Raúl Sánchez. [Así avanza la vacunación: mapas y gráficos sobre su evolución en España y el mundo](#). *El Diario* / World Bank.

#### Box 1. The problem of re-exporting vaccines.

Vaccines that have already been imported and stockpiled by a country face **three obstacles** to re-exportation.

1. The first obstacle is **logistical**: Stockpiled vaccines are closer to their expiry date. Therefore, if exported to a third country, they would enter the system with less time to be administered.
2. The second obstacle is **legal**: In the event of re-export, the vaccine manufacturer is no longer the direct supplier and therefore does not have to take legal responsibility for any problems associated with the product.
3. The third obstacle is **regulatory**: Vaccines approved in one country may not necessarily be approved in other countries.

To circumvent these obstacles, **COVAX recommends** that donations be arranged through agreements between countries and manufacturers, but with the doses transferred directly from the manufacturer to the third country (via COVAX or bilateral agreements between donor and recipient). This would mean not only that richer countries would have to forgo some of the future doses committed to them by pharmaceutical companies, but also that pharmaceutical companies would be forced to sell their vaccines to distribution mechanisms and to poorer countries at affordable prices. Eliminating the extra competition created by unnecessary third doses would go a long way towards achieving this goal.

# 3. Conclusions and Recommendations

**“The third-dose debate goes beyond the immunity arguments of particular countries. It should include a global health perspective that takes into account the bigger picture and enables decision-makers to achieve effective and equitable control of the pandemic through the rational distribution of vaccines, treatments and other measures.”**

The third-dose debate goes beyond the immunity arguments of particular countries. It should **include a global health perspective** that takes into account the bigger picture and enables decision-makers to achieve **effective and equitable control of the pandemic** through the **rational distribution** of vaccines, treatments and other measures. To develop an evidence-based roadmap with a global perspective, we recommend the following:

- a. Administer third doses only when the scientific evidence supports such a decision.** A third dose should only be offered to certain groups of immunocompromised individuals, for whom it is considered part of the normal regimen rather than a booster dose. As more evidence becomes available, it is worth considering the possibility of offering a third dose to particularly vulnerable groups, such as older adults or institutionalised people.
- b. Never organise mass booster vaccination campaigns,** as there is no clear evidence that they are necessary or that they provide substantial benefits.
- c. Ensure rational planning of vaccination campaigns.** Hoarding of vaccines by high-income countries is an unacceptable practice, as it leads to doses expiring and becoming unusable. Vaccine procurement should be planned carefully to ensure that purchases are aligned with real needs and commensurate with vaccination capacity.

- d. Global health strategy: leave no one behind.** The international community must commit to a common health strategy that addresses the challenges of the pandemic and prevents new global risks. This strategy must be supported by solid governance and the financing and delivery of vaccines with a global perspective. Besides forming the basis of the fight against the pandemic, a global health strategy can help to rebuild trust between the global North and South ●
-

## TO LEARN MORE

- Julià Blanco, Adelaida Sarukhan, Quique Bassat, Magda Campins, Robert Guerri, Carles Brotons, Juana Díez, Mireia Sans, Josep M Miró, Silvia de Sanjosé. Statement on the third dose of COVID-19 vaccines (16/09/2021). ISGlobal. September 2021.
- COVAX explained. Gavi, the Vaccine Alliance. 3 September 2021.
- Sarah Wheaton, Ashleigh Furlong. The globe's new public health strategy: Every country for itself. *Politico*. 9 September 2021.
- Covid-19 vaccine tracker: the global race to vaccinate. *Financial Times*.

## How to cite this document:


Clara Marín, Adelaida Sarukhan y Marta Rodó. Barcelona Institute for Global Health (ISGlobal). "COVID-19 and response strategy" series, no. 39. October 2021.

<https://www.isglobal.org/en/-/vacuna-covid-que-consecuencias-tiene-una-tercera-dosis-en-la-salud-global->

---

**ISGlobal** Barcelona  
Institute for  
Global Health

A partnership of:

 "la Caixa" Foundation

CLÍNIC  
BARCELONA  
Hospital Universitari

UNIVERSITAT DE  
BARCELONA

Generalitat  
de Catalunya

GOBIERNO  
DE ESPAÑA

Parc  
de Salut  
MAR

upf.  
Universitat  
Pompeu Fabra  
Barcelona

Ajuntament de  
Barcelona