Global Immunization Disparity

December 3, 2021

Abstract

The following article analyzes root causes of COVID immunization disparity at a global scale, how this inequity directly impacts rich nations, and proposes potential solutions.

Section I: Our World in Data

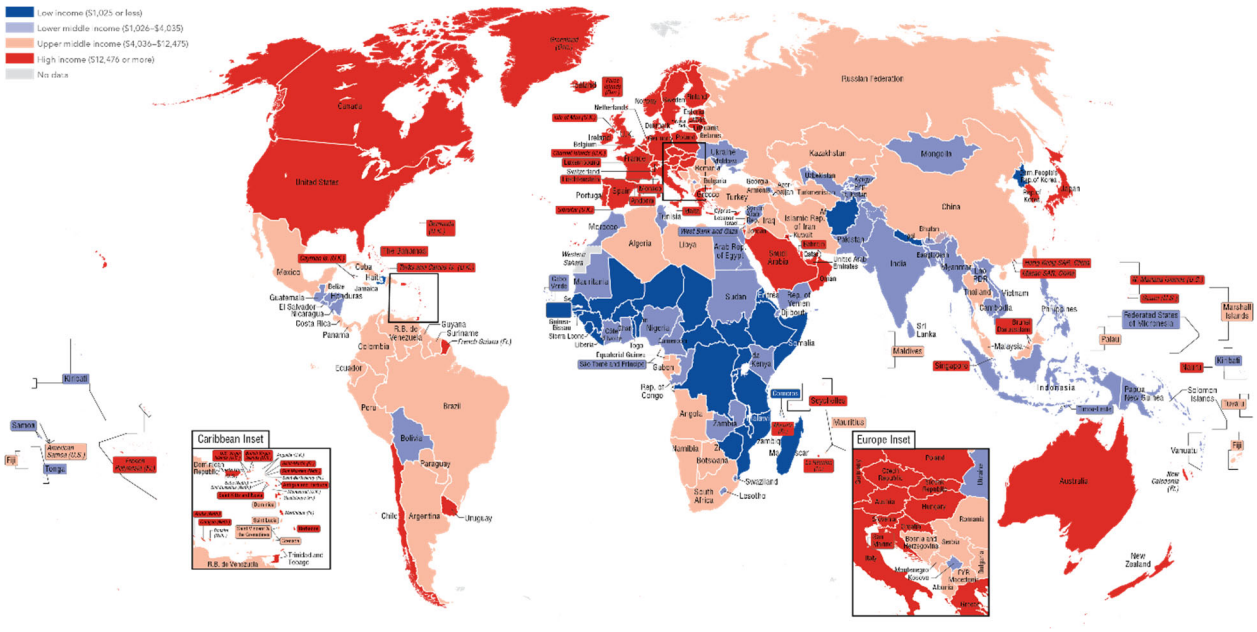
Harsh as it may sound, our world is often divided along economic data sets representing existential realities. The World Bank classifies countries into four categories: low income, lower middle income, upper middle income and high income. There is a significant income disparity between these groups. Average per capita GDP in high income country like the United States is **63 times** that of an average per capita GDP in a low-income country.

Income Group	Population (Billions)	Total Population 2020	% of World Population	2020 GDP (Trillions, USD)	Average Per Capita GDP for Income Group	Average Per Capita GDP vs. Global Average
Low Income	0.665	665,147,232	9%	0.458	$ 689	6%
Lower Middle Income	3.331	3,331,000,000	43%	7.329	$ 2,200	20%
Upper Middle Income	2.514	2,514,000,000	33%	23.105	$ 9,191	84%
High Income	1.215	1,215,000,000	16%	53.399	$ 43,950	403%
Global Totals	**7.725**	**7,725,147,232**	**100%**	**84.291**	**$ 10,911**	**100%**

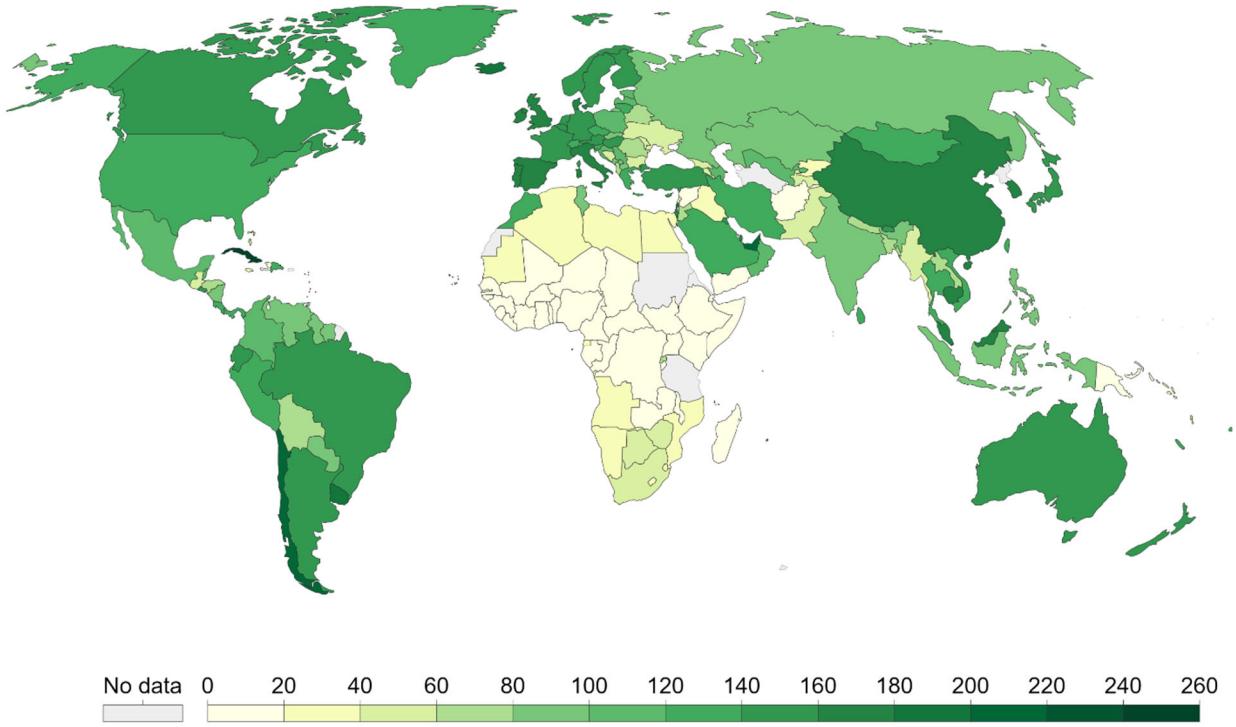
2020 Global Per Capital GDP and Population by Income Level[i]

Unfortunately, this staggering disparity is also determining who gets vaccinated first and who is last. As of December 2, 75.8% of those in high income countries had received at least one dose of the vaccine whereas only 6.2% of those in the low-income countries had received at least one dose.[ii] Based on this dataset, if you are born in a high-income country, not only do you earn 63 times as much, your likelihood of survival in a pandemic event based on immunization rate is **thirteen-fold** that of someone born in a poor country.

A simple fact of birth location determining access to lifesaving immunization is morally problematic. See the following maps of the globe for further proof of this strong relationship between immunization rate and income level. Poor countries with blue shades also have the lowest vaccination rate indicated by tan colors. Whereas wealthy, red-shaded countries also have green shades on the vaccination map indicating high COVID immunization rates. India and China are two outliers to this pattern, which will be analyzed in Section III.



Our World by Income Levels FY2017[iii]



COVID-19 Vaccine Doses Administered per 1,000 People[iv]

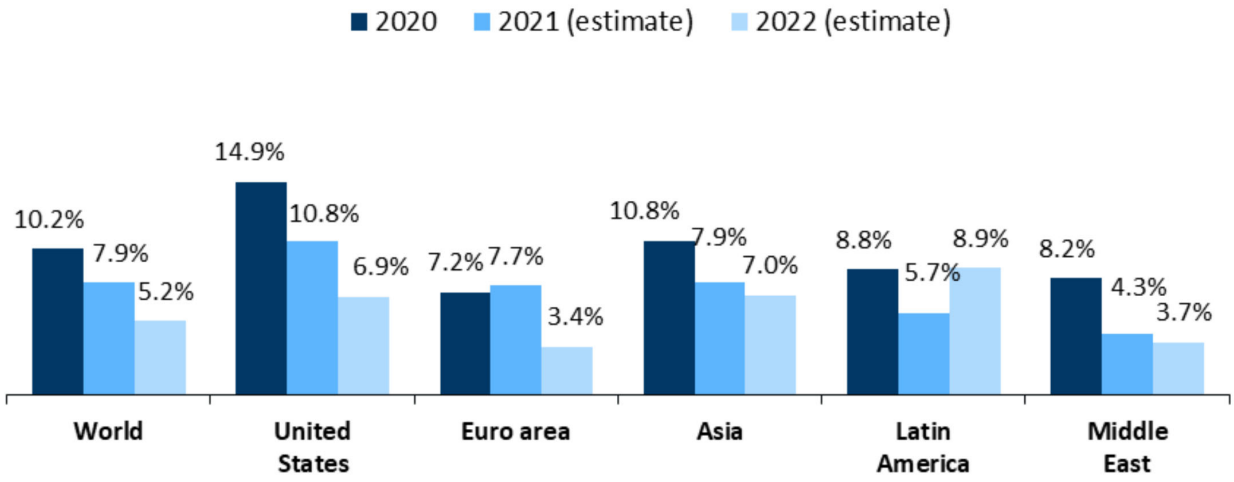
This disparity is not necessarily due to vaccine shortage at a global scale. It is estimated that we have a supply of over 10 billion doses of COVID vaccines as of today and we are producing 1.5 billion doses per month.[v] Factors such as vaccine nationalism and the tendency to ignore global nature of the pandemic are to blame.

Section II: Why Should the Rich Care?

In a globally interconnected world, quickly ending the pandemic is proving to be elusive. The virus is airborne, highly infectious and virulent. The rich nations mistakenly believe that life can go back to normal without addressing the pandemic at a global scale. Ongoing research by economists suggests it is in the financial best interest of the high-income countries to push rapid vaccination efforts at a global scale. Their argument is based on three reasons: loss of GDP, mutations, and high ROI on global vaccination.

Loss of GDP

Global GDP was projected to grow at 2.9% in 2020. Due to the pandemic, it contracted by 3.4%. Net impact is a loss of 6.3%.[vi] The GDP of the US has changed as follows: 2019 (+2.3%) 2020 (-3.4%) 2021Q1 (+1.5%) 2021Q2 (1.6%).[vii] These GDP losses are in fact much worse since the governments around the globe have injected capital into their economies by borrowing money. These drastic measures are helping to stabilize economies, however, in the process the countries are amassing large debts. In 2019, the global fiscal deficit was at 3.9% of GDP.[viii] In 2020, IMF data suggests it increased to 10.2%. The deficit is projected to remain elevated over the next few years as the economies improve.



Fiscal Deficit as a % of GDP[ix]

Wealthy nations have the most to lose due to their international trade linkages and large economies. Change in fiscal deficits due to pandemic for a few wealthy nations is as follows[x]:

United States -5.7% (2019) to -14.9% (2020) **+261%**

France -3.1% (2019) to -9.2% (2020) **+297%**

Germany +1.5% (2019) to -4.3% (2020) **+387%**

United Kingdom -2.3% (2019) to -12.5% (2020) **+545%**

China Mainland -6.3% (2019) to -11.2% (2020) **+178%**

G-20 nations have already spent $10 trillion on support during the pandemic. Nations rely heavily on the import and export of goods and services to create wealth and employment opportunities. Failure to vaccinate poor nations has global financial consequences. Economists estimate that when the dust settles, half of the total financial loss will be borne by developed nations.

ROI on Global Vaccination

Global equitable access to COVID-19 vaccines is estimated to generate economic benefits of at least US$153 billion in 2020–21 and US$466 billion by 2025 in 10 major economies, according to a new report by the Eurasia Group.[xi]

Organization for Economic Co-operation and Development (OECD) estimates that it would cost as little as $50 billion to vaccinate the world.[xii] International Chamber of Commerce (ICC) estimates the global vaccination cost to be half as much. Against this data, the return on investment (ROI) for 10 major economies is at roughly 400% in 2020-2021 and over 1,000% by 2025.[xiii] ICC estimates that the trade losses borne by the rich counties due to their international linkages could be US$0.2 trillion to US$2.7 trillion, depending on the strength of trade and production linkages.[xiv] With such a high projected ROI, concerted efforts against global immunization should be a no-brainer. We have so much to gain in the long run by simply shifting focus to global eradication efforts in the short run.

Mutations

The longer the virus stays in unvaccinated host populations, the more frequently it will mutate. With multiple mutations and less than ideal pace of vaccination, we continue to experience high mortality and infection rates from COVID-19. As of the writing of this article, more than two years since the viral outbreak, current stats indicate a fairly active pandemic state.[xv]

Daily new cases (world) approximately 700,000

Daily new deaths (world) approximately 8,000

Daily new cases (United States) approximately 140,000

Daily new deaths (United States) approximately 1,500

Mutations account for almost all of these new infections. The delta variant was discovered in India a year ago and now accounts for majority of cases in the United States. The omicron variant was detected in southern Africa in November 2021 and in just four weeks, it has spread to almost 30 countries, thanks to our global lifestyle. On November 9, we had a total of 500,000 daily infections globally and less than 1,000 daily infections within the United States. In four weeks, these numbers have grown by 200,000 and 500 respectively. Rapid spread of the variant is causing a new round of travel bans and shutdowns across the globe.

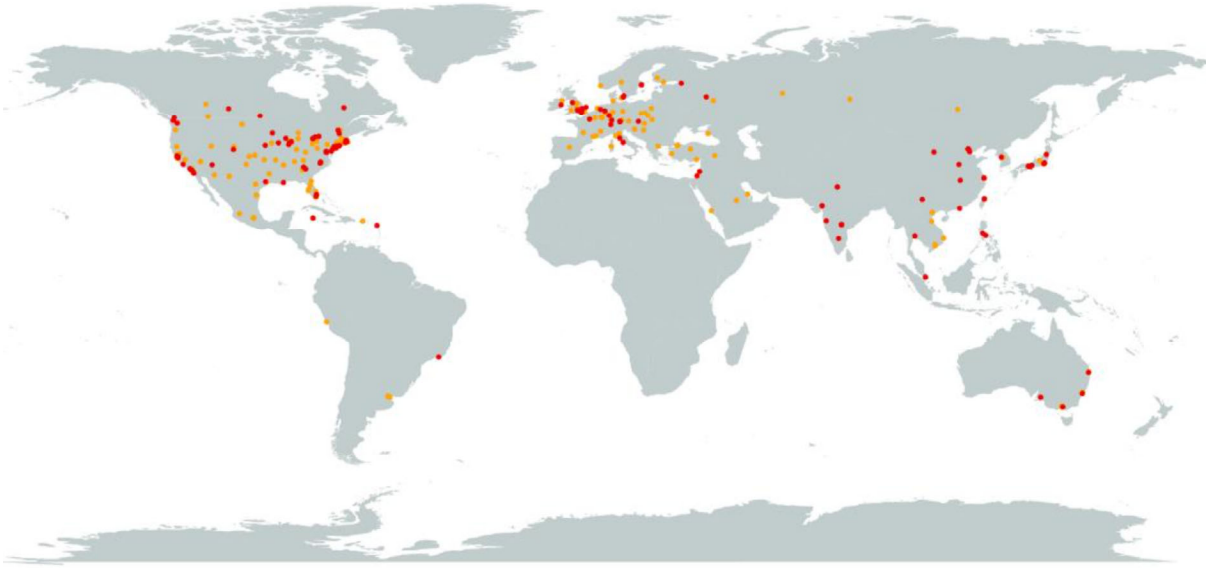
For both economic and humanitarian reasons, global immunization must be at the forefront of our collective efforts for COVID in the near term and other diseases in the long term. The World Health Organization estimates that vaccines for all preventable diseases save 2 to 3 million lives each year. The next section discusses major hurdles that we must overcome in order to achieve vaccine equity.

Section III: Challenges

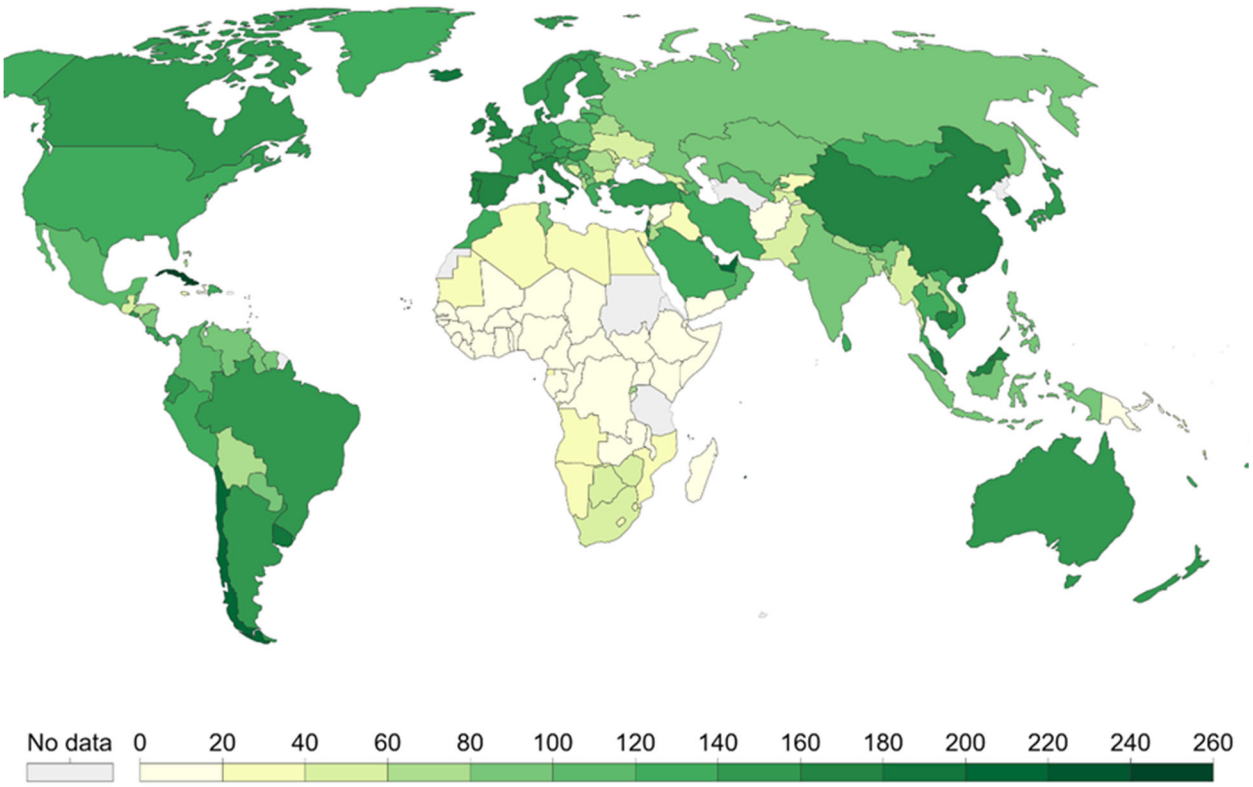
Key challenges in our battle for rapid global immunization are: lack of regional vaccine manufacturing capacity, tech transfer challenges, and high COGs (Cost of Goods).

Lack of regional manufacturing capacity:

There is a strong correlation between the capacity to manufacture vaccines locally and immunization rates. The first map below indicates locations of COVID vaccine manufacturers (red dots) and distributors (orange dots) across the globe. The second map indicates current immunization rates. Low immunization in Africa corresponds with a complete lack of local manufacturing capacity.

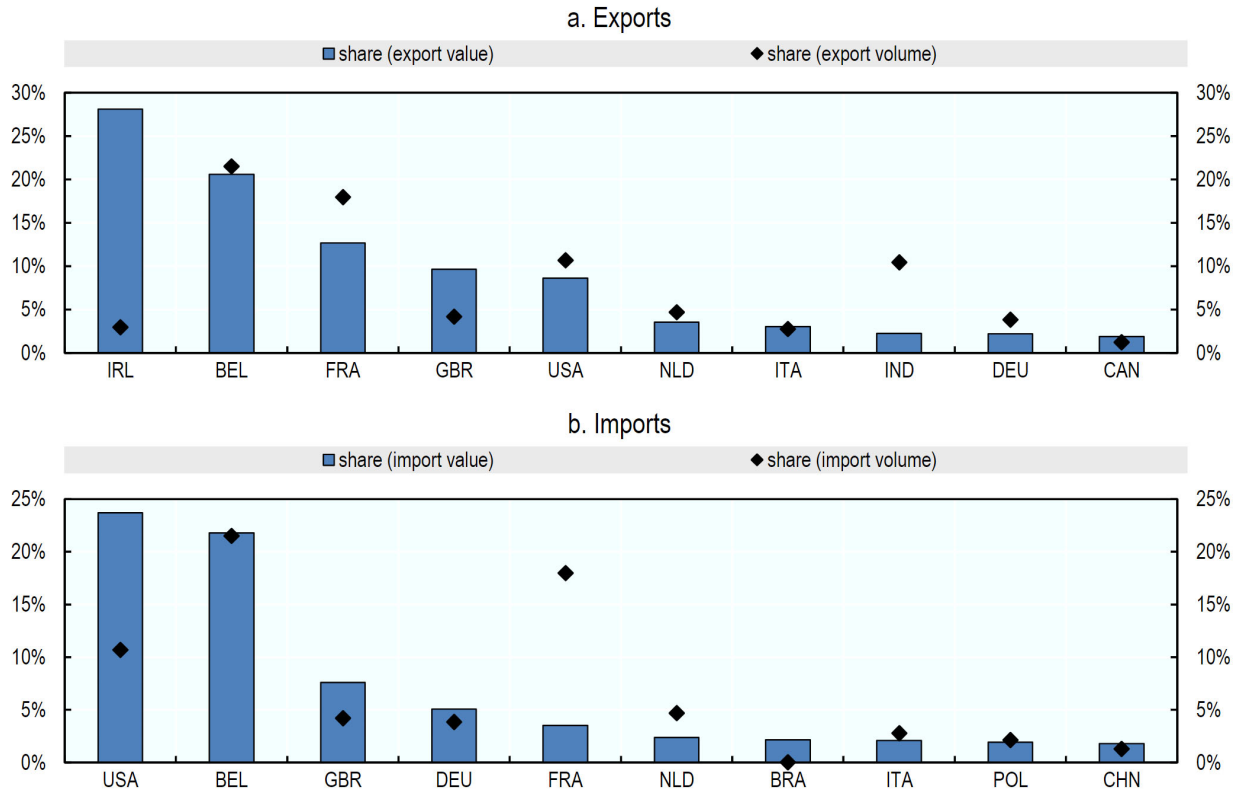


Geographic Distribution of COVID Vaccine Manufacturing and Distribution[xvi]



COVID-19 Vaccine Doses Administered per 1,000 People

This disparity is applicable to all vaccines. Only 100 countries export vaccines whereas more than twice as many import them. Moreover, the top 10 exporters account for 93% of global export value (80% in terms of volume). Ireland exports the most, with 28% by value, followed Belgium which exports 21% by value.



Share of Global Vaccine Import and Export by Values and Volumes in 2018[xvii]

With the lowest vaccination rate in the world, 99% of the vaccines administered in Africa are manufactured elsewhere. Lack of vaccine manufacturing capacity in low and low middle-income countries means that during a global pandemic, local production is not an option. Absence of regional vaccine access leads to a very slow immunization pace, prolonging the prevalence of the disease in the community. It should be noted that India and China are outliers in the sense that their immunization rates far outpace their peer countries in the same economic brackets. Strong manufacturing set-up is the only reason for their successful immunizations against COVID.

In a pandemic event, countries serve their people first and foremost. Countries with a high concentration of manufacturing capacity such as the United States are focused on controlling the regional spread of the virus. Until a country has the domestic outbreak under control, it will not shift focus towards another region. Such vaccine nationalism affects the supply chain as well. Not only do countries hoard vaccines when in dire straits, they also hold on to items such as glass vials that are critical to vaccine manufacturing and fill/finish.

As a global society we must accept this reality and focus on developing local, regionally distributed manufacturing.

Tech Transfer Challenge

Tech transfer is a term in the pharmaceutical industry when a certain medicinal product is manufactured in an alternate location, wherein the new manufacturer must prove that the product quality made in the new location matches the quality of the originally approved product. Tech transfers require intense time

commitments from developers and recipients to be successful. In 2020 the number of vaccine doses produced were well below projected counts mainly due to tech transfer challenges.

Expanding vaccine manufacturing to multiple locations is not very different from opening a second location for a top-rated restaurant. Creating a replica of a very complex product requires not only explicit knowledge such as the recipe but also tacit or intuitive knowledge that can only be gained by doing it yourself, over and over.[xviii]

The typical hurdles faced during tech transfer are as follows:

Lengthy Duration: Before COVID, most tech transfers took more than 18 months to complete and products were transferred to a single new facility. During COVID-19 many companies aimed to complete tech transfers within 6 months to as a many as 12 new facilities

Establishing Close Partnerships: Tech transfers require access to IP and know-how, as well as extensive collaboration between the developer and recipient manufacturer to ensure regulatory approval.

Regulatory Hurdles: Without adequate comparability, new companies would need to rerun clinical trials and submit new regulatory packages, adding millions of dollars and many months to the supply timelines.

Quality Control: The process at a new facility might exactly adhere to the documentation, but slight variations in raw materials such as water composition between sites could cause issues establishing analytical comparability and require costly and time-consuming action.

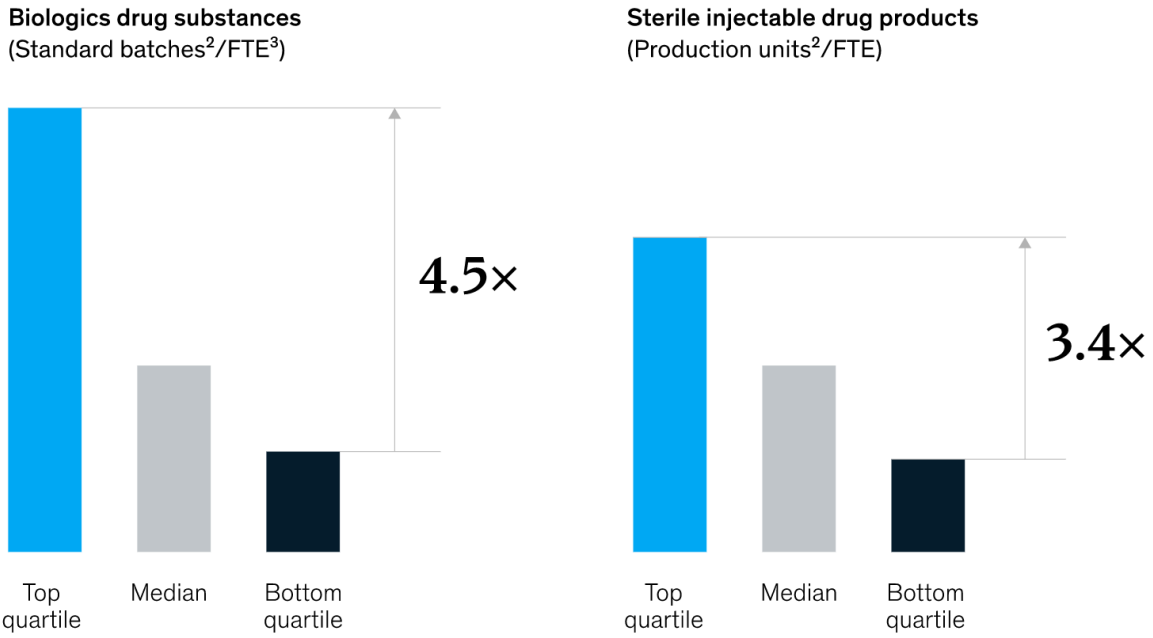
High COGs

Starting a completely new industry in a low-income country (LIC) or lower middle-income country (LMIC) such as Senegal is going to involve a large capital investment with a potential for no immediate returns. This challenge is exacerbated because LICs are at a fundamental disadvantage when it comes to manufacturing complex products such as drug substance and drug product, due to the following region-specific issues:

Demand Estimation: Unlike a mature market, LICs are undergoing significant changes in the population due to rapid growth. It is difficult to estimate an accurate demand that is required for planning a vaccine manufacturing facility. They also have a very low purchasing power and therefore rely heavily on other countries to subsidize vaccine costs. Uncertain demand and lack of financial self-reliance make it very difficult for an LIC to start a complex manufacturing industry.

Skill Shortage: A majority of the local workforce lacks education in the technical fields that is necessary for high productivity. In drug substance and drug product manufacturing, productivity is a key lever to lower costs and improve yields. COGs can see large variations, depending on the productivity of a typical full-time equivalents (FTE) at the plant. Lacking in skill and training, FTEs produce at the low range of the industry, making the COGs unfavorable for the investors.

Productivity in pharmaceutical manufacturing,[1] index (median performance = 100)



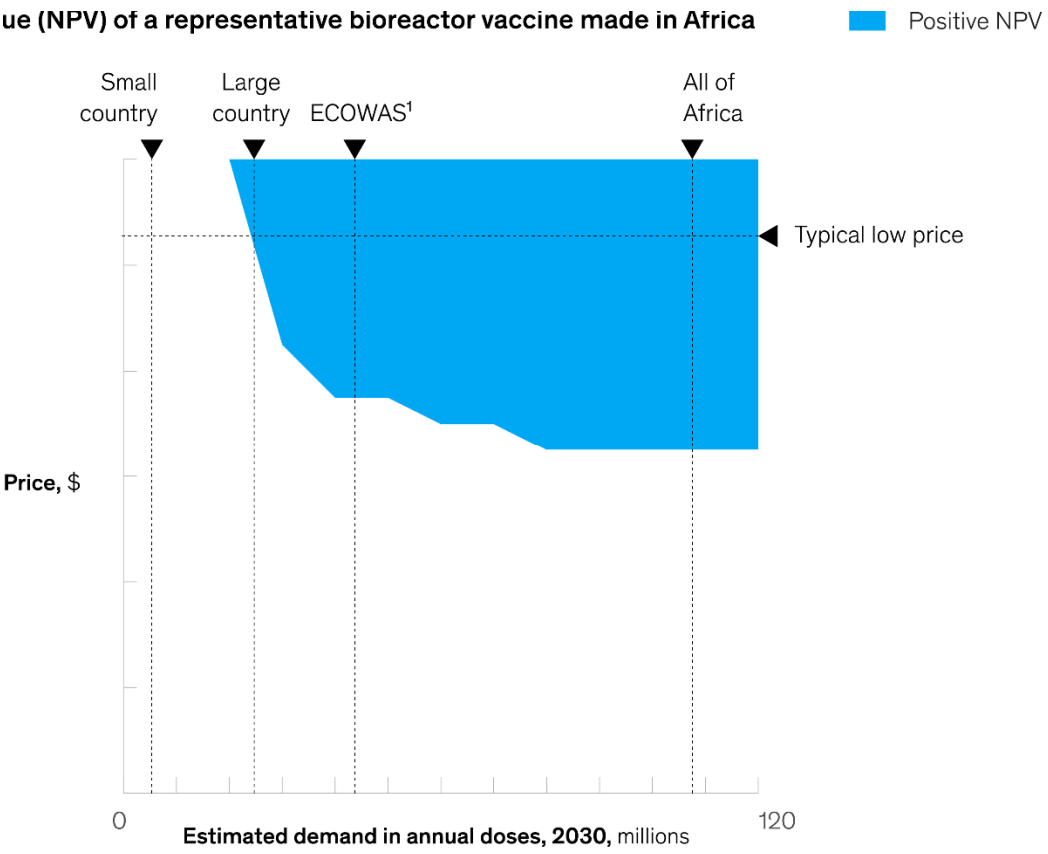
[1]McKinsey POBOS databases include more than 1,000 manufacturing plants across all regions.
[2]Standard batches and production units are normalized units used in POBOS benchmarking. Units are not comparable across technologies.
[3]Full-time equivalent.
Source: McKinsey POBOS

Productivity is a Key Lever to Lower Costs and Improve Yields[xix]

Manufacturing Technology: Technology is undergoing rapid change in the vaccine industry. Egg-based vaccines have lower costs but lower yields. Cell-culture based technologies using bioreactors have higher costs for higher yields. The latest mRNA technology has much higher costs with the highest yields. Therefore, technology has a direct impact on COGs. Finding the right technology that can be supported by local talent while achieving profitable COGs is no small feat in a LIC.

Profitability Calculator: The following chart analyzes the relationship between profitability, total production volume and unit cost of product sold. NPV or Net Present Value is the cost of dollars invested. The investment is profitable at certain sales point for a product as well as at certain minimum production volumes. The blue area is where the NPV is positive or the investment is making business sense. For an investor to be able to make money, a minimum number of dosages need to be produced. The higher the production volume, the more profitable the venture is. Similarly, as the unit cost of drugs sold increases, profit margin grows. The higher the COGs, the lower the profitability for a certain price point.

As the chart below shows there is a sweet spot when it comes to the number of doses to be produced and sold, and the cost of each dose. If we hit this range by leveraging the right technology, the cost of goods to manufacture the vaccine would make financial sense to the investors. Demand uncertainty, financial dependency, low productivity and lack of technical skill-set make it extremely difficult for LIC to hit this range of a positive NPV.



Vaccines Made in Bioreactors Can Show Positive NPV at Sufficient Scale[xx]

Section IV: LIC Centric Vaccine Strategy

LICs are fundamentally different in their population characteristics, skill sets, and infrastructure. Replicating what works in the United States or India will not work in Africa. Research indicates the following key strategies as we establish vaccine manufacturing in LICs: regionally distributed manufacturing, flexible plant design and modular vaccine technologies.

Regionally Distributed Manufacturing

Vaccine manufacturing is a very large operation requiring multiple complex steps: drug-substance manufacturing, fill/finish, packaging and labeling. To start a vaccine manufacturing plant with all of these steps together in an LIC is going to be an insurmountable task. A more practical approach would be to decouple these steps and create regions of excellence wherein drug-substance is manufactured in one location and fill/finish is done in another location.

Decentralization reduces burden on a single entity while creating more efficient operations. When a certain region focuses on one step such as drug-substance manufacturing and builds specific infrastructure and talent, it can pivot to manufacturing “vaccine adjacent” products such as mAbs or other sterile injectables. This approach maximizes utilization of the manufacturing plant and high-demand products can be made in lieu of manufacturing larger quantities without demand certainty.

With decentralization, less complex partnerships with foreign manufacturers can be established and enable faster executions. In the wake of the pandemic, several manufacturers and NGOs have committed resources and funds towards such initiatives.

Lastly, a center for excellence can be duplicated within the region once infrastructure and talent have been sufficiently developed. A scale-out vs. scale-up approach also favors modular and flexible set-up, cited as a second key strategy below.

Modular and Flexible

Technology is rapidly evolving towards modular, small-scale manufacturing. Modular platforms may be smaller in scale, but they provide the flexibility of producing at different scales. A large-scale production would simply mean building multiple lines by scaling out. These scaled out modules can produce multiple products at a small scale, if that's what the market needs. Initial investment can be smaller in terms of plant size, utilities, land and staff.

Tech transfers are easier since the initial tech transfer will take place at a smaller scale, using known platforms. Some of the most promising existing investments with proof-of-concept technologies are shown below. It should be noted that they are still under development. However, it is only a matter of time before they gain a large market share due to strong support for their implementation from the global pharmaceutical community-at-large.

Sunflower: Dahlia System
NRRV Project

JUST- Evotec Biologics : J.PODs
Infectious Disease in Low-Income markets

Univercells: Nevoline
IPV Project

Exploring and evaluating opportunities for funding

Epilogue

The pandemic has highlighted how globally interconnected our world has become. Until all nations are immunized, our lives cannot fully normalize. It has also highlighted the lack of lifesaving vaccines in the poorest parts of the world. Lastly, a healthier, more productive global population is better for business for high income countries. For these as well as humanitarian reasons, it is time to invest our excess capital into vaccine infrastructure building in the LICs.

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[i] https://data.worldbank.org/

[ii] https://ourworldindata.org/grapher/share-people-vaccinated-covid?country=High+income~Upper+middle+income~Lower+middle+income~Low+income

[iii] https://datatopics.worldbank.org/sdgatlas/archive/2017/the-world-by-income.html

[iv] https://ourworldindata.org/covid-vaccinations

[v] https://www.ifpma.org/resource-centre/momentum-of-covid-19-vaccine-manufacturing-production-scale-up-is-now-sufficient-for-step-change-in-distribution-and-opens-way-for-urgent-political-leadership-and-country-preparedness/#:~:text=Geneva%2C%207%20September%202021%3A%20Innovative,1.5%20billion%20doses%20each%20month.

[vi] https://www.statista.com/statistics/1102889/covid-19-forecasted-global-real-gdp-growth/

[vii] https://sgp.fas.org/crs/row/R46270.pdf

[viii] https://www.statista.com/statistics/1135681/global-fiscal-balance-after-coronavirus/#:~:text=Since%20the%20coronavirus%20outbreak%2C%20the,percent%20of%20the%20global%20GDP.

[ix] https://sgp.fas.org/crs/row/R46270.pdf

[x] https://data.imf.org/?sk=4be0c9cb-272a-4667-8892-34b582b21ba6

[xi] https://www.who.int/news/item/03-12-2020-global-access-to-covid-19-vaccines-estimated-to-generate-economic-benefits-of-at-least-153-billion-in-2020-21

[xii] https://www.bloomberg.com/news/articles/2021-12-01/vaccinations-key-for-recovery-would-only-cost-50-billion-oecd

[xiii] https://www.who.int/news/item/03-12-2020-global-access-to-covid-19-vaccines-estimated-to-generate-economic-benefits-of-at-least-153-billion-in-2020-21

[xiv] https://file-eu.clickdimensions.com/iccwboorg-avxnt/files/covid_vaccine_sko_nber.pdf?m=2/23/2021%208:53:24%20AM&_cldee=c2hpa2hhbWVtb3JpYWxAeWFob28uY29t&recipientid=contact-90c9da55b75dec118f8f0022489d8596-7a35fc4bb77d42d49f0645468e33e20e&esid=30c37a41-277e-458a-b395-77ebd2aa9d6a

[xv] https://www.worldometers.info/coronavirus/

[xvi] https://read.oecd-ilibrary.org/view/?ref=1060_1060354-ie4a355ojd&title=Using-trade-to-fight-COVID-19-Manufacturing-and-distributing-vaccines&_ga=2.268964977.1230094183.1638633406-2090005987.1638633406

[xvii] https://read.oecd-ilibrary.org/view/?ref=1060_1060354-ie4a355ojd&title=Using-trade-to-fight-COVID-19-Manufacturing-and-distributing-vaccines&_ga=2.268964977.1230094183.1638633406-2090005987.1638633406

[xviii] https://www.linkedin.com/pulse/what-do-vaccine-manufacturing-top-restaurants-have-common-howard/

[xix] https://www.mckinsey.com/industries/life-sciences/our-insights/africa-needs-vaccines-what-would-it-take-to-make-them-here

[xx] https://www.mckinsey.com/industries/life-sciences/our-insights/africa-needs-vaccines-what-would-it-take-to-make-them-here