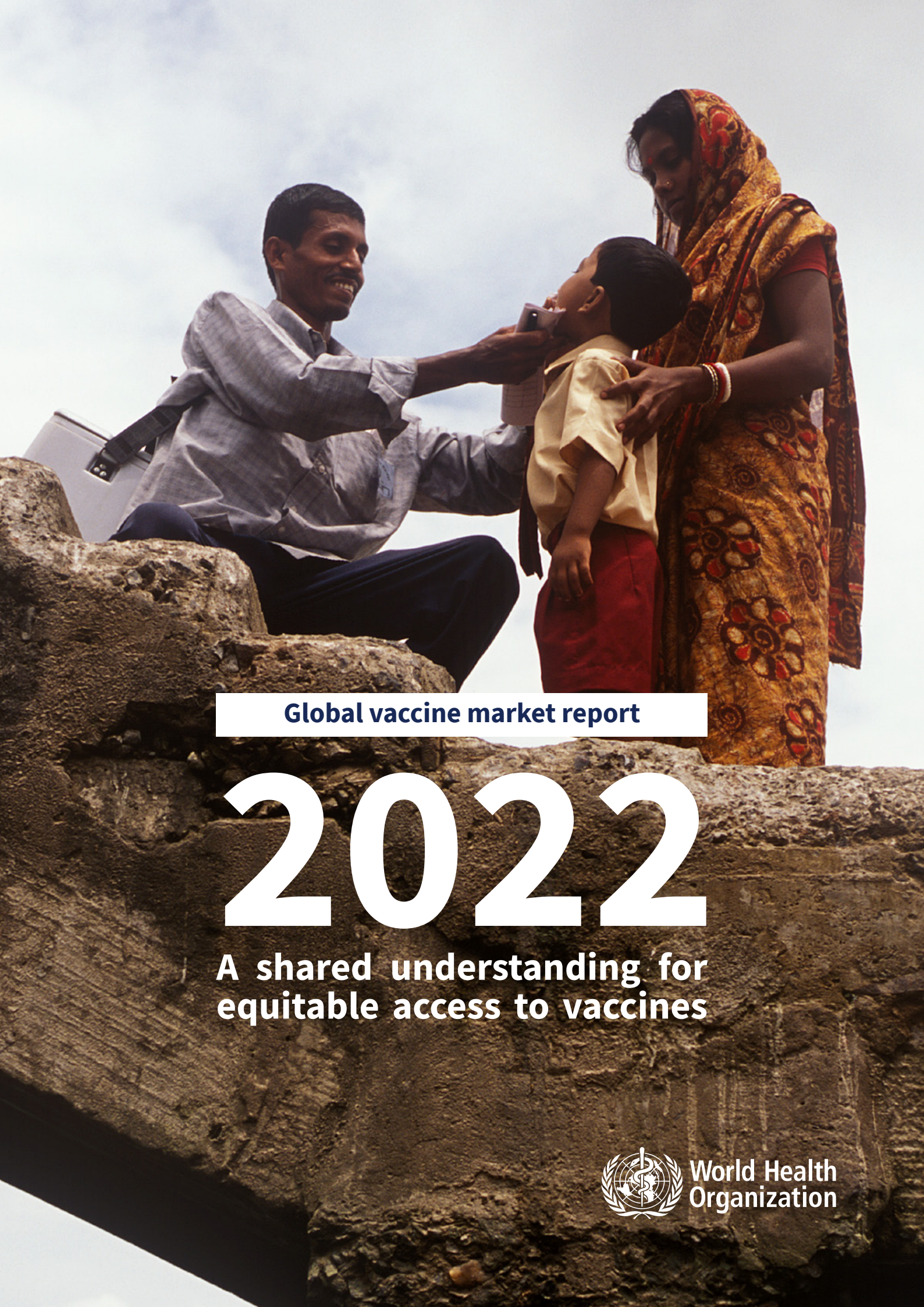

Global vaccine market report

2022

A shared understanding for equitable access to vaccines

World Health Organization

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Contents

Foreword

Immunization saves millions of lives every year and is one of the most iconic global health success stories. Yet the hard-won gains of immunization over the past two decades are at risk. Far too many people around the world still do not have access to the vaccines they need, with nearly 20 million infants missing out each year.

Using data provided primarily by WHO Member States, this Global Vaccine Market Report provides a comprehensive overview of global market dynamics in 2021 and analyses their evolution since 2019. It gives us a shared understanding of the challenges faced across the global vaccine market and sets out the actions we need to take to achieve the goals of the Immunization Agenda 2030 – the strategy adopted by the World Health Assembly in 2021 to save 50 million lives over the remainder of this decade by working towards sustainable access to vaccines for all.

While COVID-19 reminded the world of the immeasurable power of vaccines as key public goods, it also highlighted inequities in access that are sadly the rule rather than the exception globally. Lower-income countries struggle to access vaccines that are in demand across the world. For example, the human papillomavirus vaccine, which protects against cervical cancer, has been introduced in only 41% of lower-income countries, while it is saving lives in 83% of high-income countries. While prices tend to be tiered by income, further efforts are needed to alleviate pricing disparities, with middle-income countries paying as much as – or even more than – wealthier countries for several products. Regions without sizable manufacturing capacity of their own lose out and intellectual property monopolies continue to severely limit access to vaccines.

We will not recover from the historic backsliding in essential immunization if we continue to allow market dynamics alone to shape global vaccine priorities. Nor will we achieve equitable access to vaccines globally unless we have more transparency and active government oversight. We must also work to shape a more favourable intellectual property landscape and for proactive technology transfers, and to increase the building and retention of technical, manufacturing and regulatory capacity in every region.

Ultimately, we need to strike a better balance between global health objectives, national interests and commercial incentives. This can be achieved by high-level diplomacy between countries and predefined and binding rules for vaccine distribution in times of scarcity.

WHO is calling on governments, industry, international institutions and partners to act now to improve sustainable and equitable access to vaccines. I trust this report will also be used to inform ongoing negotiations on a new international accord on pandemic prevention, preparedness and response, which will allow us to respond to and end future pandemics rapidly.

Dr Tedros Adhanom Ghebreyesus
Director-General,
World Health Organization

Abbreviations

aP	acellular pertussis	**MR**	measles and rubella
BCG	Bacillus Calmette-Guérin (for tuberculosis)	**OPV**	oral polio vaccine
conj.	conjugate	**PAHO RF**	Pan American Health Organization Revolving Fund
DTaP	diphtheria–tetanus–pertussis (acellular)	**PCV**	pneumococcal conjugate vaccine
DTwP	diphtheria–tetanus–pertussis (whole cell)	**PPV23**	Pneumococcal polysaccharide vaccine, 23-valent
HepA, HepB	hepatitis A, hepatitis B	**PS**	polysaccharide
Hib	haemophilus influenzae type b	**SIA**	supplementary immunization activities
HIC	high-income country	**TBE**	tick-borne encephalitis
HPV	human papillomavirus	**TCV**	typhoid conjugate vaccine
IPV	inactivated polio vaccine	**Td**	tetanus–diphtheria (reduced antigen content)
JE	Japanese encephalitis	**TdaP**	tetanus-–diphtheria–acellular pertussis (reduced antigen content)
LIC	low-income country	**TT**	tetanus toxoid
LMIC	lower middle-income country	**UNICEF**	United Nations Children's Fund
MenA, MenB, MenC	meningococcal A, B, C	**WAP** **WHO**	weighted average price World Health Organization
MenACYW-135	meningococcal ACWY	**wP**	whole-cell pertussis
MIC	middle-income country	**YF**	yellow fever
MMR	measles, mumps and rubella	**UMIC**	upper-middle-income country
MMRV	measles, mumps, rubella and varicella		

Executive summary

The past two decades have seen important progress in access to vaccines of public health importance, with new vaccines developed and distributed globally, saving millions of lives and averting disease. Nevertheless, an extensive assessment of global vaccine market dynamics still shows significant challenges.

The many new vaccines developed against key diseases, such as meningococcal meningitis A, hepatitis E and malaria, translate into millions of lives saved. However, diseases associated with markets of little commercial value remain neglected and face suboptimal investment, few products in the development pipeline, extended timelines and delays in availability.

There is a large and expanding manufacturing base, with more than 90 manufacturers supplying vaccines to World Health Organization (WHO) Member States in 2021. However, supply remains highly dependent on fewer than 10 manufacturers with broad portfolios, global reach and a diversity of deployable technology. Even more importantly, when looking at individual vaccines, often only two or three suppliers provide most of the supply. Trends are positive, with an increased contribution of manufacturers from additional countries, but more distributed manufacturing capabilities are needed. This concentration leads to market health issues and regional supply insecurity, particularly in the WHO African and Eastern Mediterranean regions, making access to vaccines heavily dependent on the policies and supply chains of other regions.

In addition, vaccine supply has historically been unable to rapidly respond to significant changes in demand, both owing to technological challenges and to a lack of market incentives. Vaccines are typically manufactured in product-specific facilities and product changeovers are cumbersome, limiting flexibility. At the same time, manufacturing know-how, intellectual property rights protection, non-linear production costs, uncertain demand and displacing competition limit manufacturer incentives to scale up.

Coordinated procurement and financing mechanisms, particularly for lower-income settings, have reduced gaps in access, enhancing earlier availability in lower-income countries and more favourable vaccine pricing. Yet, equitable and efficient distribution of vaccines continues to suffer, as indicated by vaccines such as for pneumococcus and human papillomavirus.

On the demand side, important efforts have been made to support country planning, forecasting and budgeting: predictable country demand is key to guiding investments. However, more investment and focused effort are needed to facilitate universal vaccination with all recommended products and to enhance the diversification of the vaccines procured, increasing the reach of the vaccination programme and counter the growing threat of vaccine hesitancy. It is important that the contribution of vaccines to the well-being and prosperity of citizens is fully recognized and that clear vaccine programme priorities and objectives are set, proper planning is executed and budgetary appropriations are made accordingly.

The COVID-19 pandemic has given unprecedented visibility to vaccine market dynamics and has shown that some of these challenges can be overcome.

The vaccine community made new vaccines available in less than one year while using innovative technology platforms that enabled faster scalability. This achievement resulted from unprecedented public investment, early and parallel at-risk investment in clinical development and manufacturing capacity and the streamlining of regulatory processes. Those factors, combined with the size of the population targeted by COVID-19 vaccines, led to a three-fold increase in vaccine doses procured globally within 12 months.

This incredible achievement in the face of a public health emergency of international concern made stark the long-standing need to reconsider the value of vaccines as a fundamental and cost-effective public good rather than a commodity. We must acknowledge both that vaccines are under-invested and that free-market dynamics do not optimize for social and health impact. Without strong public engagement, the strategic focus and investments of manufacturers will remain limited relative to the need for an ambitious immunization agenda and will continue to concentrate on more profitable pharmaceutical interventions and on high-income market vaccines.

COVID-19 has also shown that large public investment, streamlined processes, new technologies, pooled financing and procurement are not sufficient to achieve optimal public benefit. Efficient and equitable access to COVID-19 vaccines has been highly problematic as a result of dynamics repeatedly experienced in other vaccine markets. The lack of transparency along the value chain of vaccine manufacturing and distribution and the lack of government oversight made it hard for governments to plan and use vaccines most efficiently within national boundaries as well as across countries. Despite the impressive number of approximately 15 billion doses delivered globally through various mechanisms as of October 2022, COVAX accounted for only 12% of this volume, indicating that serving all populations more equitably and ending future pandemics requires more than financing and procurement efforts. We need to enhance government oversight of vaccine production and distribution and strike a much better balance between serving national interests and global public health objectives. The only means to achieve this is through high-level diplomacy between countries and pre-defined and binding rules for vaccine distribution at a time of scarcity. We also must work on a more favourable intellectual property landscape, proactive technology transfers and the building and retention of local technical and regulatory capacity. We should acknowledge that additional dedicated and permanent manufacturing capacity is costly and should be valued not only as means to satisfy current vaccine demand but also as an insurance against future public health needs *(1)*.

We have an opportunity to establish a new paradigm for vaccine development and access that builds on new practices and some of the lessons learned during the COVID-19 pandemic. This new paradigm could be incorporated as part of a new international accord on pandemic prevention, preparedness and response. In this new paradigm, we call for stakeholders to assume their shared but differentiated responsibilities; that is, for governments to commit to:

1. Establish early, evidence-informed strategic goals and leadership that serve the collective global health interest and to shoulder risks and invest aggressively in order to address the needs of today and prepare for future emergencies.
2. Strengthen market preparedness by investing in new vaccine technologies, regional research and development and manufacturing hubs, and by enabling regulatory harmonization.
3. Ensure transparency and oversight along the vaccine value chain towards enhanced health impact, as well as, define principles and operational mechanisms for collaboration across countries in times of scarcity, including for intellectual property and the circulation of inputs and goods.

We call on industry to commit to:

1. Ensure that activities are aligned with WHO's guidance: research and development efforts focused on the WHO list of priority pathogens and target product profiles, more clinical trials performed in low-income countries, and targeted to inform global policy needs and expedited data submissions for regulatory approvals and prequalification.
2. Establish provisions for technology transfer and ensure transparency along the vaccine value chain.
3. Commit to specific measures allowing for equity-driven allocation of products.

And we call on international organizations and partners to commit to:

1. Prioritize the achievement of global public health priorities as per the Immunization Agenda 2030 as an umbrella for individual organizational strategies, priorities and interests.
2. Support country-driven initiatives and projects consistently with organizations' missions and avoid the creation of duplicate efforts.
3. Continue to call for technology transfer and for the application of resolutions on market transparency for health products.

In the next pandemic, this paradigm would serve both equity and national interests by reducing disease everywhere through a faster, more coordinated and more equitable global response. Between pandemics, this paradigm would enable bolder, coordinated leadership to improve access to vaccines for all.

Preface

The Market Information for Access Initiative (MI4A) was launched in 2018 to contribute to the achievement of Strategic Development Goal 3.8 (Universal Health Coverage target) by enhancing access to safe, effective, quality and affordable vaccines for all. This important matter has been highlighted by the World Health Assembly in 2019 with the endorsement of a Roadmap for Access to medicines and vaccines, the adoption of resolution WHA 72.8 on improving the transparency of markets for medicines, vaccines and other health products.

MI4A is a peer platform that leverages data collected from countries and provides the data publicly to inform product choice, conduct financial planning, optimize budgets, enhance procurement and strengthen national, regional and global capacity for improved access to vaccines. Vaccine manufacturers also participate by sharing information on their late-stage pipeline and available supply, as well as by engaging in dialogue to inform investment decisions.

More information on MI4A can be found below: Immunization, Vaccines and Biologicals (who.int)

The 2022 Global Vaccine Market Report uses data provided by the Member States and other publicly available sources *(1)*. The volumes and value data referred to in this report are based primarily on doses purchased by countries as reported through the MI4A initiative leveraging the World Health Organization–United Nations Children's Fund (UNICEF) electronic Joint Reporting Form and represent the doses distributed to countries. WHO Member States and vaccines irrespective of their financing or procurement channel and regulatory approval status are included.

The report aims to capture lessons from the COVID-19 pandemic and to highlight the opportunity for more ambitious global action: expanding sustainable access to vaccines for all towards the Immunization Agenda 2030 and pandemic prevention, preparedness and response efforts. The report is organized in two sections: the first section provides WHO insights on global vaccine market dynamics, drawing from data provided by Member States, which are, in turn, analysed and displayed in the second section.

1. Revenues for public companies were accessed via Evaluate – www.evaluate.com – in August 2022.

Photo: WHO / Asad Zaidi

Section 1

A shared understanding for equitable access to vaccines

Vaccine portfolio and regulation

KEY POINT

Significant progress has been achieved in the development of new vaccines against key diseases, although diseases associated with markets with less commercial value remain neglected. COVID-19 proved that vaccines can be developed even faster through large public investments, joint planning of clinical development, regulation and manufacturing capacity and leveraging innovative platforms.

Significant progress has been achieved in the development of new vaccines against important diseases that primarily affect lower-income countries

The global vaccine portfolio has been expanding over the past decades, with the development of new vaccines against diseases that primarily affect lower-income countries (such as meningococcal meningitis A, hepatitis E, dengue fever, Ebola, malaria) in addition to those targeted at more affluent countries. Several of those vaccines were enabled by philanthropic organizations, public institutions, nongovernmental organizations and public–private partnerships *(2-3)*.

COVID-19 proved that vaccines can be developed in a very short time when stakeholders make a concerted effort

Political pressure dramatically reduced the time in which vaccines were developed, reducing, in turn, the human and economic impact of the disease *(4)*. Academic institutions, biotech firms, pharmaceutical companies, military research units and state-owned actors redirected their efforts to identifying suitable technologies and moved vaccine candidates quickly through clinical development, registration, commercialization and distribution *(5-6)*. A process that takes an average of 10 years and has never taken less than four years was compressed to 11 months *(7-8)*.

» **A process that takes an average of 10 years and has never taken less than four years was compressed to 11 months.**

Large public investments and joint planning of clinical development, regulation, manufacturing capacity and innovative platforms were key enablers for fast vaccine development

While this entailed a much higher level of financial risk *(9-10)*, there was no compromise on safety and COVID-19 vaccines have been submitted for approval with larger data sets than is typically seen for other vaccines. Early, continuous and transparent engagement between regulators and vaccine developers and collaboration among regulators led to emerging questions and issues being addressed more efficiently *(11-14)*. The positive impact of those efforts is reflected in a growing number of suppliers and of vaccines available for use: in less than two years the number of different COVID-19 vaccines available is second only to seasonal influenza (see Annex 1 for more information on the number of vaccines available per disease).

Even before the emergence of COVID-19, work on viral-vectored platforms, including the Ebola vaccine, could be quickly leveraged, allowing vaccine development based on genetic sequence information alone. In addition, because they can be used for multiple targets, those technology platforms can be considered as candidates for unique approaches to regulation across multiple vaccines *(15)*. Finally, those innovative platforms are highly adaptable and can speed up vaccine development considerably *(16)*. As happened with modern vaccine platforms in the past decades, the weight of innovative platforms is set to increase in the coming years (see Annex 1 for more information on platform categorization).

Years of harmonization efforts, mutual reliance schemes and strengthening of local regulatory capacity led to a fast response to the COVID-19 pandemic; even so, regulatory processes remain challenging

Vaccines are medical products that are routinely administered to healthy people, and, as a result, real or perceived quality issues can compromise trust in immunization, rapidly erasing progress *(17)*. This understanding makes quality assurance a critical aspect for vaccination. Regulatory strengthening and harmonization progressed significantly in response to the needs of the COVID-19 pandemic. Ten COVID-19 vaccines achieved WHO Emergency Use Listing Procedure by 2021 *(18)*. This unprecedented achievement leveraged years of harmonization efforts, mutual reliance schemes and strengthening of local regulatory capacity *(19)*.

Over the past decades, regulatory agencies and regional networks helped to strengthen regulatory capacity and improve cross-country regulatory coordination *(20)*, resulting in a broader geographical reach of newly developed vaccines. Through its prequalification programme, WHO has been providing regulatory assistance to countries procuring through United Nations agencies. WHO has also supported countries to develop stable, well-functioning and integrated regulatory systems *(21)* with streamlined processes and predictable timelines *(22-24)*. WHO has classified the national regulatory authority in 35 vaccine-producing countries at a sufficient maturity level (level 3 or 4) to provide oversight of vaccine development, manufacturing and release. Two new countries have

matured to this level since 2019 (see the Vaccine Regulation paragraph of the Data and Analysis section).

Even so, regulatory processes remain challenging. Regulatory experts, manufacturers, WHO and other stakeholders have highlighted the divergence in vaccine registration requirements worldwide and pointed to the need for stepping up convergence initiatives, reliance and improving pharmacovigilance *(25)*. Aligning to this regulatory divergence is more cumbersome for manufacturers in developing countries, potentially limiting access to the more affordable products *(26-28)*.

For markets with less commercial value, we still face suboptimal investment and few pipeline products, extended timelines and delays in availability

Diseases such as hookworm, schistosomiasis and leishmaniasis *(29)*, and diseases and pathogens prioritized by the WHO R&D Blueprint, such as Zika, Lassa fever, Nipah and henipaviral diseases, Rift Valley fever, Crimean–Congo haemorrhagic fever and filoviruses *(30)*, are still missing a vaccine.

In the past decade, several mechanisms have been launched to provide guidance on product suitability and value, helping private entities to assess commercial opportunities and public health needs when investing in development and manufacturing *(31)*. While helpful, this guidance does not provide assurance that demand will materialize, even for products that meet targets. The size and likelihood of the demand become clear only after the completion of clinical development, well after key decisions on product presentations and manufacturing capacity must be made. As a result, we still face suboptimal investment, few products in the development pipeline, extended timelines and delays in availability for markets with less commercial value *(32)*. This is especially evident for the WHO African, South-East Asia and Eastern Mediterranean regions, which represent important volumes of vaccine use, largely owing to demographics, but not a great share of market value (see the Market Size paragraph of the Data and Analysis section).

Manufacturing base

KEY POINT

Despite a large and growing number of manufacturers, the vaccine supply base remains highly concentrated, leading to market health issues and regional supply security implications

As of 2021, the vaccine supplier base includes a large and growing number of manufacturers

Based on data reported, more than 90 manufacturers supplied vaccines to WHO Member States, 10 of which entered the market in response to the COVID-19 pandemic. The manufacturing base is growing as a result of investments in new vaccines, national manufacturers for large countries, such as Brazil, China, India and the Russian Federation, looking beyond domestic markets, the expansion of the WHO prequalification programme and strategic procurement by the Pan American Health Organization (PAHO) and the United Nations Children's Fund (UNICEF) *(33-35)*. China and India, where 31% of global manufacturers are headquartered in 2021, have seen manufacturing capacity increase.

Despite this large base vaccine, manufacturing remains highly concentrated

According to country data, globally, 10 manufacturers alone provide 70% of vaccine doses (excluding COVID-19 vaccines) and 85% of the global value of vaccines. More importantly, when looking at individual vaccines, often only two or three suppliers provide more than 80% of supply. More than half of suppliers globally produce only a few vaccines and only serve local markets (see the Manufacturing and Supply paragraph of the Data and Analysis section).

Concentration of manufacturing has clear causes: vaccine development and manufacturing have high costs of entry and normally yield lower profits relative to the entry costs and compared to other pharmaceutical products. In 2021, approximately 16 billion doses of 47 different vaccines, with an estimated value of US$ 141 billion, were distributed worldwide. This almost three-fold increase over the market volume in 2019 and 3.5-fold increase in market value was primarily driven by the advent of COVID-19 vaccines (see the Market Size paragraph of the Data and Analysis section). Nevertheless, vaccines continue to represent a mere 4% of the overall pharmaceutical market (10% if we account for COVID-19 vaccines). Risks of failure and economies of scale also contribute to supplier concentration *(36)*. Lastly, potential product liability, since vaccines are administered to healthy people, can be seen as a disincentive to entry *(37)*.

Supply concentration leads to concerns on market health for key high-impact vaccines

Each of the human papillomavirus, pneumococcal conjugate and measles, mumps and rubella combination vaccines is used by at least 100 countries, but each market is highly dependent on one or two manufacturers that account for more than 80% of vaccines by volume. The health of markets for six vaccines potentially needed in the event of an emergency, demand for which may surge during a disease outbreak, is also concerning (see the Market health and Regional supply security paragraphs of the Data and analysis section).

In addition, the manufacturing base is only in certain geographical areas: beyond China and India, vaccine manufacturers are mostly located in the European Union, Indonesia, Japan and the United States of America. Lack of production capacity in various regions raises regional supply security concerns much discussed over the past decade and during the COVID-19 crisis: the African and Eastern Mediterranean regions remain dependent on manufacturers headquartered elsewhere for 90% of their procured vaccines *(38)*. The World Trade Organization negotiations over the long-sought intellectual property waiver for COVID-19 vaccines pointed to the need for further dialogue on ways to ensure faster and more distributed production *(39)*.

» **The African and Eastern Mediterranean regions remain dependent on manufacturers headquartered elsewhere for 90% of their procured vaccines.**

Historically, vaccine supply has been unable to respond rapidly to significant changes in demand

Changes in demand are typically linked to the release of a new vaccine or the issuance of a global vaccination strategy, or to disease outbreaks. Some examples include past shortages of products such as human papillomavirus vaccines and inactivated polio vaccines *(40-42)*.

These supply constraints are in part due to the technologies currently used in vaccine manufacturing. Vaccines are complex biological products and not accounting sufficiently for the complexity of process scale-up can lead to delays in availability. Vaccines are typically manufactured in product-specific facilities and product changeovers are cumbersome, limiting flexibility. Increasing capacity requires significant lead times and financial investment. Technology transfer and changes in manufacturing technologies and processes can address these limitations but are costly and take time, while the quality assurance and regulatory review processes required to ensure that changes do not affect the quality of the final product also contribute to complexity *(43-44)*.

COVID-19 has taught us a lesson: the production of vaccines can be scaled-up with unprecedented speed by leveraging new technology platforms

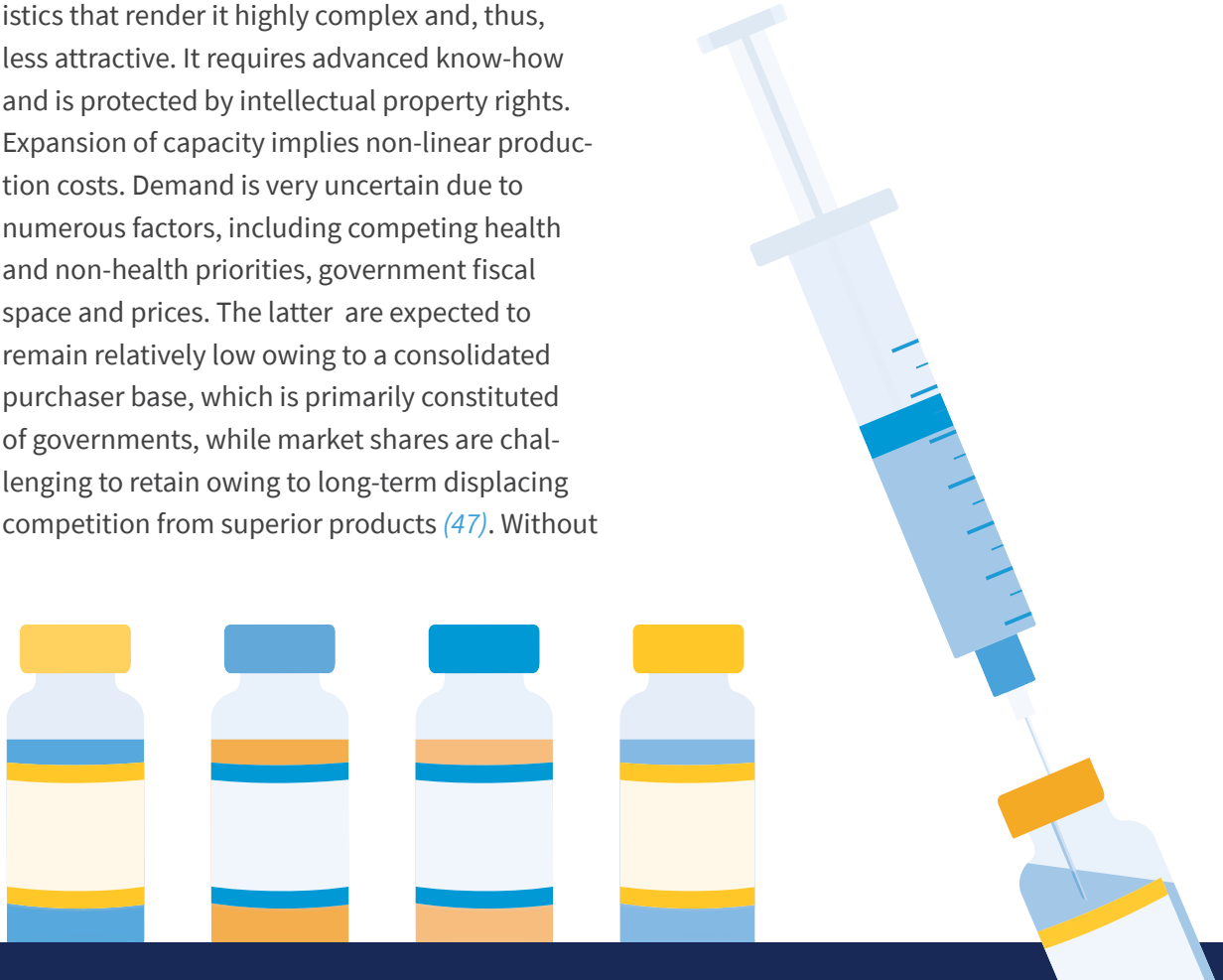
New platforms enable vaccines to be produced by incorporating genes for different proteins with little or no alteration in the manufacturing process or components. This provides for manufacturing to be more easily scaled, adjusted

and repurposed for use with new products: a paradigm shift for an industry that usually dedicates one building or production area to each vaccine *(45)*. Among COVID-19 vaccines used in 2021, 36% were designed using innovative technologies and accounted for 59% of global volumes of COVID-19 vaccine procured by WHO Member States. Those innovative technologies have a large potential but are still in their infancy, as evidenced by their very limited use other than for COVID-19 vaccines (see the Manufacturing and Supply paragraph of the Data and Analysis section).

Large public contracts to build vaccines manufacturing capacity and guarantee of purchase made a significant difference *(46)*

The vaccine market has a number of characteristics that render it highly complex and, thus, less attractive. It requires advanced know-how and is protected by intellectual property rights. Expansion of capacity implies non-linear production costs. Demand is very uncertain due to numerous factors, including competing health and non-health priorities, government fiscal space and prices. The latter are expected to remain relatively low owing to a consolidated purchaser base, which is primarily constituted of governments, while market shares are challenging to retain owing to long-term displacing competition from superior products *(47)*. Without incentives, companies would have limited interest in investing in large manufacturing plants. Unprecedented use of partnerships has enhanced manufacturing bulk production, access to proprietary adjuvants and final product fill and finish *(48-51)*.

We should acknowledge the efforts that led manufacturers to make more than 10 billion doses of COVID-19 vaccine available by the end of 2021 *(52)*, while acknowledging that even more could have been done to meet larger global public health needs and support ambitious timelines for equitable vaccine deployment set by countries *(53-57)*. Mainstreaming those successes and learnings outside of the unique circumstances of a pandemic will be necessary to address several of the shortcomings emerging in the vaccine ecosystem and highlighted in this report.



Allocation of scarce supply

KEY POINT

Equitable and efficient distribution of vaccines both within and across national boundaries requires a much higher level of transparency, public oversight over production and distribution, commitment from manufacturers and high-level diplomacy between countries

In addition to increasing their investments in vaccine development and manufacturing, COVID-19 taught us that governments could have played a more active role in the oversight of vaccine supply

The need for more transparency was pointed out by many during the COVID-19 pandemic *(58-59)*. Plans for the production of COVID-19 vaccines, allocation amounts and delivery dates have been unclear. Lacking oversight, governments struggled to make informed, rapid and strategic decisions on the effective distribution of vaccines within national borders, especially in the first 12 months of vaccine availability. To strike a careful balance between rewarding private investments and fair and predictable access for purchasers, governments need more transparency in manufacturing costs, capacity, contracts, and operations; among others, they need to be able to ensure licensing and technology transfer to enable increased production, as well as set up compensation schemes where appropriate.

Inequitable distribution, although not unique to COVID-19 vaccines *(60)*, was a moral and global security failure with health and economic consequences

Lack of equity in access to COVID-19 vaccines, particularly in the African and Eastern Mediterranean Regions, is especially problematic. The African region represents one fifth of the global population, but in 2021 the region received just 3% of all COVID-19 vaccine doses. While COVID-19 received unprecedented attention, it is important to understand that dynamics related to inequitable vaccine distribution across countries are not unique (albeit at a different scale). Among vaccines that are relevant for global use, access in lower-income settings remains limited.

» **The African Region represents one fifth of the global population, but in 2021 the region received just 3% of all COVID-19 vaccine doses.**

» **We need to strike a much better balance between serving national interests, global public health objectives and commercial incentives. The only means to achieve this is through high-level diplomacy between countries and commitment to a new paradigm.**

Historically, vaccine development costs and capital investments are recouped through higher-priced sales in high-income countries, and only thereafter vaccines are made available to lower-income countries at lower prices and in large volumes *(61)*. While there has been substantial progress over the past 20 years with the PAHO Revolving Fund, UNICEF and Gavi, the Vaccine Alliance, ensuring predictable funding and streamlined procurement processes *(62-63)*, the data from countries show that constraints and uneven access in the use of paediatric vaccines continues: rotavirus vaccine is used in only 58% of self-procuring middle-income countries; similarly, human papillomavirus vaccine is used in only 41% of lower-income countries, despite those countries representing a large proportion of cervical cancer burden and having more limited access to other prevention and curative services. Also, life-course vaccination, defined as vaccination given through all phases of life, a key priority for the Immunization Agenda 2030, is limited outside of higher-income countries, where more than 80% of adult vaccine doses (excluding COVID-19 vaccines) are distributed (see the Market health and Regional supply security paragraphs of the Data and analysis section).

COVAX reinforced the lessons that serving all populations more equitably and ending future pandemics more rapidly cannot be achieved just through financing and procurement mechanisms

More than 180 countries have signed on to the COVAX Facility and countries with constrained resources have been served by the pooling mechanism. Approximately 15 billion doses of COVID-19 vaccine being shipped to October 2022 *(64)*. Nevertheless, and in spite of COVAX efforts to coordinate global demand and supply for equitable distribution *(65-66)*, most contracted volumes have sat outside of the Facility, with the latter accounting for only 12% of the total volume of deliveries to date, while lower income countries have been left behind.

The COVID-19 pandemic also showed that key innovations were driven by publicly supported investments in research institutions, basic science discoveries, national health institutes and direct funding of product development in different countries. However, access to life-saving innovations such as vaccines were not available to all who need them in a timely and equitable manner, including because of intellectual property monopolies. In addition to the effect on pricing, intellectual property continues to limit the possibility of leveraging fully the capacity to produce and supply locally and regionally in lower-income countries. We need to strike a much better balance between serving national interests, global public health objectives and commercial interests. The only means to achieve this is through high-level diplomacy between countries, and commitment to a new paradigm.

Country demand for vaccines

KEY POINT

Predictable country demand is key to guiding investments, therefore efforts should be focused on enhancing its predictability by tackling affordability, planning and procurement issues, and by boosting political will and fortifying health systems

Country demand predictability has been a major obstacle to vaccine access, while affordability is often portrayed as an important cause for low demand

Compared to other pharmaceuticals, supply of vaccines is largely publicly funded through government and pooled procurement mechanisms. Private sector procurement has only a limited size. Concentrated demand should help plan investments for the required supply. Nevertheless, predictability of demand remains a key issue for access.

Affordability has often made the headlines in the media as one of the prominent factors that limit demand. Price dynamics have remained generally unchanged over the past years and despite prices being tiered between country income groups, wide price ranges exist, and overlap between tiers, revealing opportunities for price streamlining. For example, differences are as high as 19-fold for the Bacillus Calmette–Guérin vaccine and about 15-fold for human papillomavirus and hepatitis B vaccines across upper-middle-income countries (see the Pricing and Procurement paragraph of the Data and Analytics section).

Root causes for limited and unpredictable country vaccine demand, particularly from lower-income settings, range from insufficient political will to inadequate infrastructure and market segmentation due to different products

While price has been a highly debated issue, the root causes for at times limited and very often unpredictable country vaccine demand, particularly from lower-income settings, are more wide-ranging. These include unclear vaccine agendas and scattered planning, insufficient political will and fiscal space to increase health budgets, unpredictable decision-making and planning, ineffective procurement and weaknesses in immunization programmes and overall health systems *(67-68)*. Funding and procurement delays on the demand side are the most frequently reported causes that have led to

» **Pooled procurement attains lower prices for 14 of the 18 vaccines most widely used in middle-income countries, the average price for all 18 vaccines combined being 42% lower.**

national shortages of vaccines (see the Global distribution paragraph of the Data and analytics section).

The increasing market segmentation resulting from the growing availability of vaccines with differing product characteristics and diverging country preferences has an especially negative impact on demand predictability. Low-income and middle-income countries need both a greater ability to inform product development and manufacturing scale-up for preferred products and access to the evidence needed to make trade-off decisions. Vaccines deemed functionally equivalent by WHO still have distinct characteristics and may not be operationally interchangeable. As a result, markets for pneumococcal conjugate and human papillomavirus, rotavirus and pertussis vaccines are segmented, and a preferred vaccine may be in short supply even when the total availability is sufficient *(69-72)*. Product preferences can have negative consequences when they delay introductions and therefore require careful consideration *(73)*.

Global and regional efforts are attempting to tackle demand issues through funding and pooled procurement

Public–private partnerships and United Nations agencies have stepped in to fund and procure on behalf of lower-income countries some 15% of the global volume purchased (but a minimal share of the total value in 2021) (see the Pricing and procurement paragraph of the Data and analysis section). Compared to self-procurement, pooled procurement attains lower prices for 14 of the 18 vaccines most widely used in middle-income countries, the average price for all 18 vaccines combined being 42% lower, although differences vary significantly for individual vaccines. Low-income countries are almost exclusively pool-procuring, but the average price for the top 12 vaccines combined is 21% lower than pooled procured prices for the same vaccines in middle-income countries. New initiatives in this area are being explored by the African Union (with the launch of the African Vaccine Acquisition Trust), small island developing states, the Association of Southeast Asian Nations, Eurasian Economic Union countries and the South-Eastern European Health Network *(74-77)*.

Investment and focused efforts are needed to facilitate universal vaccination and enhance the diversification of the vaccines procured and to increase the reach of the vaccination programme and counter vaccine hesitancy

More limited attention and work have been devoted to address the shortcomings on the demand side compared to the work done on the supply side. As a consequence of the difficulty to predict demand early enough, and in addition to the political challenge of securing financing for a medical product that delivers its return often with a significant time interval since the investment (and with no tangible measure of success other than the absence of disease), informed investments and risk-sharing decisions are challenging to implement.

Overall, more investment and focused effort are needed to facilitate universal vaccination with all recommended products and to enhance the diversification of the vaccines procured, support increasing the reach of the vaccination programme and counter vaccine hesitancy. It is important that the full contribution of vaccines to the well-being and prosperity of citizens is recognized and that clear vaccine programme priorities and objectives are set, proper planning is executed and budgetary appropriations are made accordingly.

Conclusions and call for action

The past two decades have seen important progress in access to vaccines of global public health importance, with new vaccines developed and distributed globally, saving millions of lives and averting disease. Nevertheless, an extensive assessment of global vaccine market dynamics still shows significant challenges, with research and development gaps and delays, regulatory barriers, manufacturing limitations, unequitable access and unpredictable and fragmented country demand.

The COVID-19 pandemic has exposed the unmeasurable public health value of vaccines. We have an opportunity to establish a new paradigm for vaccine development and access that builds on new practices and some of the lessons learned during the recent pandemic. This new paradigm should be incorporated as part of a new international accord on pandemic prevention, preparedness and response. In this new paradigm, we call for stakeholders to assume their shared but differentiated responsibilities.

We call on governments to commit to:

1

Establish **early, evidence-informed strategic goals and leadership** that serve the collective global health interest and to **shoulder risks and invest aggressively** in order to address the needs of today and prepare for future emergencies.

2

Strengthen market preparedness by investing in new vaccine technologies, regional research and development and manufacturing hubs, and by enabling regulatory harmonization.

3

Ensure transparency and oversight along the vaccine value chain towards enhanced health impact, as well as define principles and operational mechanisms for collaboration across countries in times of scarcity, including particularly for intellectual property and the circulation of inputs and goods.

We call on industry to commit to:

1

Ensure that activities are aligned with WHO's guidance: research and development efforts focused on the WHO list of priority pathogens and target product profiles, more clinical trials performed in low-income countries, and targeted to inform global policy needs and expedited data submissions for regulatory approvals and prequalification.

2

Establish provisions for technology transfer and ensure transparency along the vaccine value chain.

3

Commit to specific measures allowing for equity-driven allocation of products.

We call on international organizations and partners to commit to:

1

Prioritize the achievement of global public health priorities as per the Immunization Agenda 2030 as an umbrella for individual organizational strategies, priorities and interests.

2

Support country-driven initiatives and projects consistently with organizations' missions and avoid the creation of duplicate efforts.

3

Continue to call for technology transfer and for the application of resolutions on market transparency for health products.

In the next pandemic, this paradigm would serve both equity and national interests by reducing disease everywhere through a faster, more coordinated and more equitable global response.

Between pandemics, this paradigm would enable bolder, coordinated leadership to improve access to vaccines for all.

1. Castillo JC, Ahuja A, Athey S, Baker A, Budish E, Chipty T, et al. Market design to accelerate COVID-19 vaccine supply. Science. 2021;371:1107-9. doi: 10.1126/science.abg0889.

2. World Health Organization. An R&D blueprint for action to prevent epidemics. 2016. (https://www.who.int/publications/i/item/who-research-and-development-blueprint-evaluation-of-ideas-for-potential-platforms-to-support-development-and-production-of-health-technologies-for-priority-infectious-diseases-with-epidemic-potential, accessed February 8, 2022).

3. Coalition for Epidemic Preparedness Innovations. CEPI 2022-2026 strategy. 2021. https://cepi.net/wp-content/uploads/2021/03/CEPI-2.0_Strategy-2022-26-Mar21.pdf [accessed April 1, 2021].

4. WHO coronavirus (COVID-19) dashboard. Geneva: World Health Organization; 2022 (https://covid19.who.int, accessed 24 March 2022).

5. World Health Organization. Draft landscape and tracker of COVID-19 candidate vaccines. 2021. (https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines, accessed March 19, 2021).

6. UNICEF Supply Division. COVID-19 vaccine market dashboard. https://www.unicef.org/supply/covid-19-vaccine-market-dashboard [accessed March 28, 2021].

7. UNICEF Supply Division. COVID-19 vaccine market dashboard. https://www.unicef.org/supply/covid-19-vaccine-market-dashboard [accessed March 28, 2021].

8. World Health Organization. WHO issues its first emergency use validation for a COVID-19 vaccine and emphasizes need for equitable global access. 2020. (https://www.who.int/news/item/31-12-2020-who-issues-its-first-emergency-use-validation-for-a-covid-19-vaccine-and-emphasizes-need-for-equitable-global-access, accessed March 24, 2022).

9. Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. Lancet. 2021;397:1023-34. doi: 10.1016/S0140-6736(21)00306-8.

10. Black S, Bloom DE, Kaslow DC, Pecetta S, Rappuoli R. Transforming vaccine development. Semin Immunol. 2020;50:101413. doi: 10.1016/j.smim.2020.101413.

11. World Health Organization. WHO-ICMRA joint statement on the need for improved global regulatory alignment on COVID-19 medicines and vaccines. 2020. (https://www.who.int/news/item/06-11-2020-who-icmra-joint-statement-on-the-need-for-improved-global-regulatory-alignment-on-covid-19-medicines-and-vaccines, accessed April 6, 2021).

12. United States National Library of Medicine. ClinicalTrials.gov https://clinicaltrials.gov/ct2/results/map?term=vaccine&type=Intr&cond=COVID-19&map [accessed March 24, 2022].

13. Guzman J, O'Connell E, Kikule K, Hafner T. The WHO global benchmarking tool: a game changer for strengthening national regulatory capacity. BMJ Glob Health. 2020;5. doi: 10.1136/bmjgh-2020-003181.

14. International Coalition of Medicines Regulatory Authorities (ICMRA). ICMRA 2021 summit and plenary meeting report. 2021. https://www.icmra.info/drupal/sites/default/files/2022-01/ICMRA_Summit_and_Plenary_2021_Meeting_Report.pdf [accessed March 24, 2022].

15. Adaljia AA, Watson M, Cicero A, Inglesby T. Vaccine platforms: state of the field and looming challenges. Johns Hopkins Bloomberg School of Public Health Center for Health Security, 2019. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2019/190423-OPP-platform-report.pdf [accessed March 28, 2021].

16. van Riel D, de Wit E. Next-generation vaccine platforms for COVID-19. Nat Mater. 2020;19:810-2. doi: 10.1038/s41563-020-0746-0.

17. World Health Organization. Prioritizing diseases for research and development in emergency contexts. (https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts, accessed April 1, 2021).

18. COVID-19 vaccines with WHO emergency use listing | WHO - prequalification of medical products (IVDs, medicines, vaccines and immunization devices, vector control).

19. World Local Production Forum: enhancing access to medicines and other health technologies, report of the first World Local Production Forum, 21–25 June 2021. Geneva: World Health Organization; 2021.

20. Mihigo R, Okeibunor J, Cernuschi T, Petu A, Satoulou A, Zawaira F. Improving access to affordable vaccines for middle-income countries in the African region. Vaccine. 2019;37:2838-42. doi: 10.1016/j.vaccine.2019.03.077.

21. Khadem Broojerdi A, Baran Sillo H, Ostad A, Dehaghi R, Ward M, Refaat M, Parry J. The World Health Organization Global Benchmarking Tool: an instrument to strengthen medical products regulation and promote universal health coverage. Front. Med. 2020;7:457. doi: 10.3389/ fmed.2020.00457.

22. World Health Organization. Delivering quality-assured medical products for all. WHO's five-year plan to help build effective and efficient regulatory systems. 2019. (https://www.who.int/medicines/news/2019/WHO_ActionPlan.pdf, accessed April 6, 2021).

23. World Health Organization. Global vaccine market report. 2020. (https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2020_Global_Vaccine_Market_Report.pdf?ua=1, accessed September 14, 2021).

24. World Local Production Forum: enhancing access to medicines and other health technologies, report of the first World Local Production Forum, 21–25 June 2021. Geneva: World Health Organization; 2021.

25. Dellepiane N, Pagliusi S, Registration experts working group. Challenges for the registration of vaccines in emerging countries: differences in dossier requirements, application and evaluation processes. Vaccine. 2018;36:3389-96. doi: 10.1016/j.vaccine.2018.03.049.

26. Dellepiane N, Pagliusi S, Registration experts working group. Challenges for the registration of vaccines in emerging countries: differences in dossier requirements, application and evaluation processes. Vaccine. 2018;36:3389-96. doi: 10.1016/j.vaccine.2018.03.049.

27. Hayman B, Bowles A, Evans B, Eyermann E, Nepomnyashchiy L, Pagliusi S. Advancing innovation for vaccine manufacturers from developing countries: prioritization, barriers, opportunities. Vaccine. 2021;39:1190-4. doi: 10.1016/j.vaccine.2020.12.085.

28. WHO MIC Task Force. Sustainable access to vaccines in middle-income countries (MICs): a shared partner strategy. 2015. (https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Apr2015/7_session_middle_income_taskforce/Apr2015_session7_vaccines_in_MICs.pdf, accessed March 29, 2021).

29. Hotez PJ. The global fight to develop antipoverty vaccines in the anti-vaccine era. Hum Vaccin Immunother. 2018;14:2128-31. doi: 10.1080/21645515.2018.1430542.

30. World Health Organization. Prioritizing diseases for research and development in emergency contexts. (https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts, accessed April 1, 2021).

31. WHO preferred product characteristics (PPCs).

32. Cernuschi T, Malvolti S, Hall S, Debruyne L, Pedersen HB, Rees H, et al. The quest for more effective vaccine markets – opportunities, challenges, and what has changed with the SARS-CoV-2 pandemic. Vaccine. 2022. doi: 10.1016/j.vaccine.2022.07.032.

33. Parry J. China enters the global vaccine market. Bull. World Health Organ. 2014;92:626-7. doi: http://dx.doi.org/10.2471/BLT.14.020914.

34. World Health Organization. Prequalified vaccines. (https://extranet.who.int/pqweb/vaccines/prequalified-vaccines, accessed March 28, 2021).

35. UNICEF Supply Division Annual Report. Copenhgen: UNICEF, 2021 (https://www.unicef.org/supply/supply-annual-report-2021)

36. World Health Organization. Global vaccine market report. 2020. (https://www.who.int/publications/m/item/2020-who-global-vaccine-market-report, accessed September 14, 2021).

37. Danzon P, Pereira NS. Why sole-supplier vaccine markets may be here to stay. Health Aff (Millwood). 2005;24:694-6. doi: 10.1377/hlthaff.24.3.694.

38. Framework for Action. Partnership for African Vaccine Manufacturing, 2021 (https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/)

39. Ministerial decision on the TRIPS Agreement. https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True.

40. Sutter RW, Zaffran M. Addressing the inactivated poliovirus vaccine shortage. Lancet. 2019;393:2569-71. doi: 10.1016/S0140-6736(19)30766-4.

41. du Preez K, Seddon JA, Schaaf HS, Hesseling AC, Starke JR, Osman M, et al. Global shortages of BCG vaccine and tuberculous meningitis in children. Lancet Glob Health. 2019;7:e28-e9. doi: 10.1016/S2214-109X(18)30474-1.

42. Garland SM, Stanley MA, Giuliano AR, Moscicki AB, Kaufmann A, Bhatla N, et al. IPVS statement on "Temporary HPV vaccine shortage: Implications globally to achieve equity". Papillomavirus Res. 2020;9:100195. doi: 10.1016/j.pvr.2020.100195.

43. GVAP Secretariat Report 2013, page 80 (https://ia601809.us.archive.org/35/items/WHO-documents/2013_WHO_global_vaccine_action_plan-GVAP_secretariat_report_2013.pdf)

44. WHO Vaccine Supply and Quality Unit GPV policy statement on vaccine quality (https://apps.who.int/iris/handle/10665/63578).

45. Adaljia AA, Watson M, Cicero A, Inglesby T. Vaccine platforms: state of the field and looming challenges. Johns Hopkins Bloomberg School of Public Health Center for Health Security, 2019. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2019/190423-OPP-platform-report.pdf [accessed March 28, 2021].

46. Agarwal R, Gaule P. What drives innovation? Lessons from COVID-19 R&D. IZA Institute of Labor Economics, 2021. http://ftp.iza.org/dp14079.pdf [accessed March 29, 2021].

47. World Health Organization. C-19 Vaccine price data from publicly available information and as reported by countries to WHO. 2022. (https://cdn.who.int/media/docs/default-source/immunization/mi4a/price-analyses-covid-19-vaccines.pdf, accessed March 24, 2022).

48. Abinader LG. Manufacturers of COVID-19 vaccines typically start delivering in under six months after tech transfer. https://www.keionline.org/35364 [accessed April 1, 2021].

49. Newmarker C. Baxter to make Moderna COVID-19 vaccine in US. MassDevice.2021. https://www.massdevice.com/baxter-to-make-moderna-covid-19-vaccine-in-us/ [accessed April 1, 2021].

50. Elgot J. UK to make up to 60m doses of Novavax covid vaccine under GSK deal. The Guardian. https://www.theguardian.com/world/2021/mar/29/uk-strikes-deal-gsk-doses-novavax-covid-vaccine [accessed April 1, 2021].

51. GSK. Developing COVID-19 vaccines. https://us.gsk.com/en-us/media/covid-19-response-and-updates/#tab-1-1 [accessed April 1, 2021].

52. Launch and scale faster. Vaccine manufacturing. The murky manufacturing landscape. https://launchandscalefaster.org/covid-19/vaccinemanufacturing [accessed April 1, 2021].

53. United Nations. Secretary-General calls vaccine equity biggest moral test for global community, as Security Council considers equitable availability of doses. 2021. https://www.un.org/press/en/2021/sc14438.doc.htm [accessed April 1, 2021].

54. Fore H, Ghebreyesus TA. In the COVID-19 vaccine race, we either win together or lose together. 2021. https://www.who.int/news/item/10-02-2021-in-the-covid-19-vaccine-race-we-either-win-together-or-lose-together [accessed April 1, 2021].

55. Multilateral leaders task force on COVID-19. https://www.covid-19taskforce.com/en/programs/task-force-on-covid-19-vaccines [accessed March 24, 2022].

56. Ahuja A, Athey S, Baker A, Budish E, Castillo JC, Glennerster R, et al. Preparing for a pandemic: accelerating vaccine availability. Becker Friedman Institute for Economics at the University of Chicago, 2021. https://bfi.uchicago.edu/wp-content/uploads/2021/02/BFI_WP_2021-08.pdf.

57. Cernuschi T, Malvolti S, Downham M, Maugeais D, Robinson D, Cravioto A. COVID-19 impact on infant and adolescent vaccine supplies. Science. 2021;374:1438-41. doi: 10.1126/science.abl7019.

58. Transparency International. COVID-19 Vaccine Transparency. 2021. https://www.transparency.org/en/news/covid-19-vaccine-transparency# [accessed April 1, 2021].

59. Kenny C. Release COVID-19 vaccine contracts. Center for Global Development. https://www.cgdev.org/blog/release-covid-19-vaccine-contracts [accessed April 1, 2021].

60. World Health Organization. Global COVID-19 vaccination strategy in a changing world: July 2022 update. (https://www.who.int/publications/m/item/global-covid-19-vaccination-strategy-in-a-changing-world--july-2022-update, accessed October 10, 2022).

61. Makinen M, Kaddar M, Molldrem V, Wilson L. New vaccine adoption in lower-middle-income countries. Health Policy Plan. 2012;27 Suppl 2:ii39-49. doi: 10.1093/heapol/czs036.

62. UNICEF. Scaling vaccine procurement. 2020. https://www.unicef.org/supply/stories/scaling-vaccine-procurement [accessed March 26, 2021]

63. Clemens J, Holmgren J, Kaufmann SH, Mantovani A. Ten years of the Global Alliance for Vaccines and Immunization: challenges and progress. Nat Immunol. 2010;11:1069-72. doi: 10.1038/ni1210-1069.

64. Source: Delivery estimates are generated from recorded deliveries from public sources, COVAX/AVAT delivery data from UNICEF, and estimated deliveries based on administered doses from OWID. The values may not reflect actual deliveries

65. Médecins Sans Frontières Access Campaign. COVAX: A broken promise to the world. 2021. https://msfaccess.org/sites/default/files/2021-12/COVID19_IssueBrief_Covax_1708_ENG_21.12.2021.pdf [accessed March 24, 2022].

66. World Health Organization. An allocation framework for fair and equitable access to COVID-19 health products. 2020. (https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Apr2016/7_session_vaccine_shortage/Apr2016_session7_vaccine_supply_shortages.pdf, accessed March 24, 2022).

67. Berkley S. Vaccination lags behind in middle-income countries. Nature. 2019;569:309. doi: 10.1038/d41586-019-01494-y.

68. Immunization Agenda 2030. Middle-income countries. 2021. https://www.immunizationagenda2030.org/resources/33-middle-income-countries [accessed March 19, 2021].

69. UNICEF Supply Division. Human papillomavirus vaccine: supply and demand update. 2020. https://www.unicef.org/supply/media/5406/file/Human-Papillomavirus-Vaccine-Market-Update-October2020.pdf [accessed March 9, 2021].

70. World Health Organization. V3P: Key findings for rota. 2018. (https://www.who.int/publications/m/item/v3p--key-findings-for-rota, accessed March 28, 2021).

71. UNICEF Supply Division. Pentavalent vaccine (DTPwP-HepB-Hib): Market & Supply Update. 2017. https://www.unicef.org/supply/media/541/file/Pentavalent%20vaccine(DTwP-HepB-Hib)%20market%20and%20supply%20update.pdf [accessed May 28, 2020].

72. UNICEF Supply Division. Pneumococcal conjugate vaccine: supply and demand update. 2020. https://www.unicef.org/supply/media/4636/file/Pneumococcal-conjugate-vaccine-supply-update-July2020.pdf [accessed March 28, 2021].

73. World Health Organization. Pre-empting and responding to vaccine supply shortages. 2016. (https://www.who.int/immunization/sage/meetings/2016/april/1_Mariat_shortages_SAGE_2016.pdf?ua=1Some, accessed March 28, 2021).

74. Swails B, McSweeney E. African Union secures 270 million extra covid vaccine doses for the continent. CNN.com.2021. https://www.cnn.com/2021/01/14/africa/vaccine-africa-intl/index.html [accessed March 19, 2021].

75. South Eastern European Health Network. http://seehn.org/ [accessed March 19, 2021].

76. McEvoy E, Ferri D. The role of the joint procurement agreement during the COVID-19 pandemic: assessing its usefulness and discussing its potential to support a European health union. Eur. J. Risk Reg. 2020;11:851-63. doi: https://doi.org/10.1017/err.2020.91.

77. Gulf Health Council. Gulf joint procurement program. http://ghc.sa/en-us/Pages/gpintro.aspx [accessed April 1, 2021].

Photo: WHO / Andrew Esiebo

Section 2

Data and analysis

Key notes for the reader

The 2021 market is analysed, first including and then excluding COVID-19 vaccines. Subsequently, the 2021 market excluding COVID-19 vaccines is compared to the 2019 market. The purpose is to highlight the market shift since 2019 and how much of this shift can be attributed to the COVID-19 pandemic. Where appropriate, separate analyses of the 2021 COVID-19 vaccine market are performed.

Volume data represent the doses distributed to countries, and as such they should not be interpreted as country consumptions or as the production or capacity of manufacturers. The value data represent the volume multiplied by the acquisition cost/price of the vaccine by the end purchaser. Differences in the timing and recording of purchase and sales data representing 2021 are not fully aligned across all sources and are approximated.

Vaccines are grouped into six categories based on their primary target population: (1) vaccines used for children/adolescents (Children/Adolescents); (2) vaccines used primarily for adults (Adult); (3) vaccines used for diseases with a regional/local burden or for diseases of sporadic occurrence (Local/Sporadic), while vaccines used for paediatric populations are split based on their geographical reach: (4) paediatric vaccines used worldwide (WW Ped); (5) paediatric vaccines used primarily in lower- and lower-middle-income countries (LMIC Ped); and (6) paediatric vaccines used primarily in high-income countries (HIC Ped). More detailed information on the methodology can be found in Annex 1.

Market size

Based on country reported data, WHO estimates that, across 47 vaccines and 94 manufacturers, the 2021 global vaccine market supplied approximately 16 billion vaccine doses (up from 5.8 billion in 2019), with a value of US$ 141 billion (up from US$ 38 billion in 2019). This value accounts for 10% of the pharmaceutical market (up from 4% in 2019). Without COVID-19 vaccines, the 2021 vaccine market supplied approximately 5.3 billion doses, with a value of US$ 42 billion and 4% of the pharmaceutical market – the minor changes compared to 2019 result from decreased volumes of some paediatric vaccines and increased volumes of some (higher price) adult vaccines.

In 2021, COVID-19 and seasonal influenza vaccines, and oral polio vaccine (OPV) used in supplemental immunization activities (SIAs), had the largest volumes. The top 10 vaccines by volume, each with a volume of at least 200 million doses, accounted for 92% of global volume (Fig. 1). The increase in market size from 2019 to 2021 was almost entirely driven by the introduction of COVID-19 vaccines, which accounted for more than double the volume and value of all other vaccines distributed in 2021.

COVID-19, seasonal influenza and pneumococcal conjugate (PCV) vaccines have the highest global value. COVID-19 and seasonal influenza vaccines have relatively high prices and high volumes owing to their large target populations, while PCV has very high prices, particularly in high-income countries (HICs), despite lower volumes. The top 10 vaccines represent 90% of market value when including COVID-19 vaccines and 75% of market value when excluding those (Fig. 2).

Fig. 1: Vaccines by volume (doses), 2021

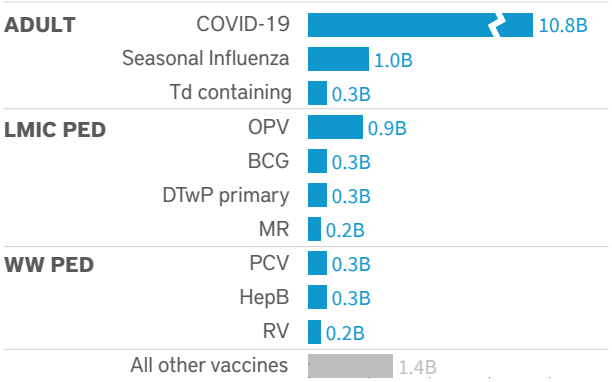
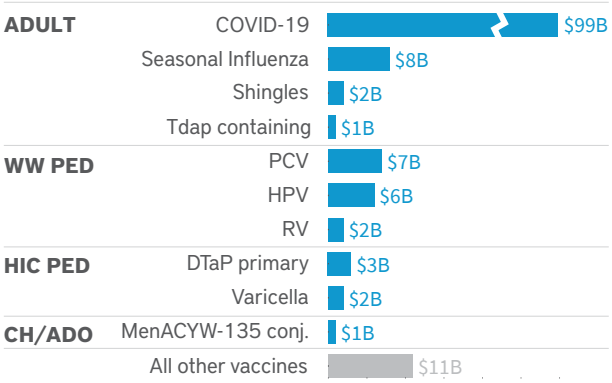


Fig. 2: Vaccines by value ($), 2021



When examining volume and value by vaccine category, adult vaccines, including for COVID-19, represent three quarters of the 2021 volume; all paediatric vaccines comprise 20% of the global volume; children/adolescent vaccines and local/sporadic are the remaining 5% of volume. Compared to 2019, adult vaccine volumes showed a nine-fold increase due to COVID-19 vaccines. Non-COVID-19 adult vaccine volumes increased by 15% due to an increased use of seasonal influenza vaccines in HICs. All paediatric vaccine volumes declined by 14% compared to the pre-pandemic baseline of 2019, driven by decreased use of OPV and measles–rubella vaccine (MR) in SIAs (Fig. 3).

Comparing volume and value by region reveal patterns. The South-East Asia Region and the WHO Western Pacific Region are the largest regions by volume of vaccine distributed, accounting for more than half the doses of vaccines, with China (22%) and India (17%) the largest countries. The WHO Region of the Americas and Western Pacific regions are the largest by value, exceeding 60% of total value. The United States (21%) and China (15%) are the highest-value countries, driven by good access to COVID-19 vaccines and high prices, the use of adult vaccines in the United States and a significant private paediatric vaccine market with high prices in China. When excluding COVID-19 vaccines, the value of Region of the Americas and

Fig. 3: Volume change from 2019 by vaccine category (COVID-19 excluded)

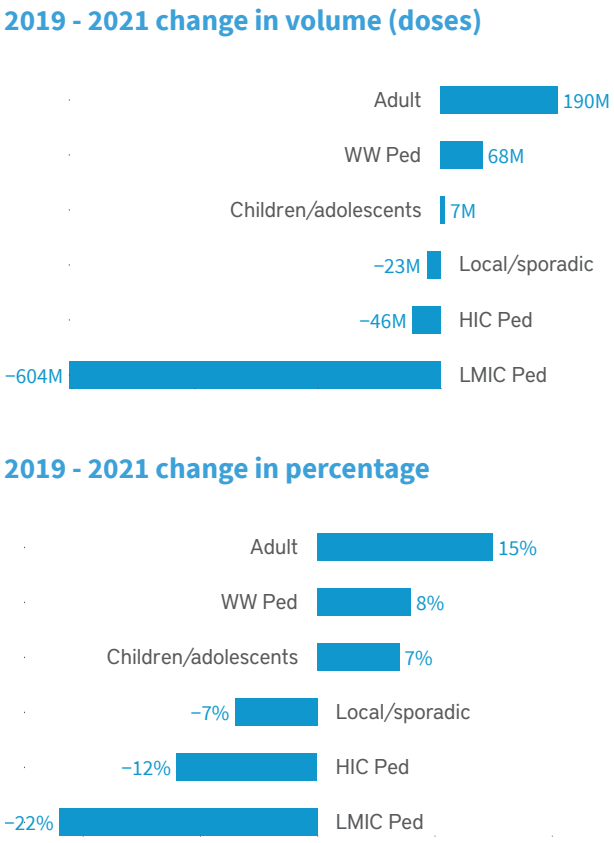


Fig. 4: Volume and value by region, 2021

	VOLUME		VALUE	
	With COVID-19	Excluding COVID-19	With COVID-19	Excluding COVID-19
African Region	8%	17%	3%	3%
Region of the Americas	18%	15%	34%	47%
South-East Asian Region	24%	27%	10%	3%
European Region	13%	12%	20%	20%
Eastern Mediterranean Region	7%	10%	5%	4%
Western Pacific Region	30%	18%	28%	24%

Western Pacific Region increases to more than 70% of the global market (Fig. 4). Compared to 2019, the African Region volume share declines as a result of poor access to COVID-19 vaccines and decreases in the volumes of paediatric vaccines.

The analysis of value variations by vaccine category and region completes the picture. When taken together, paediatric vaccines, at 44% of the total, are the highest value segment of the market (excluding COVID-19 vaccines), owing to their widespread adoption. Adult vaccines are the highest value segment in the Region of the Americas and the WHO European regions because of high prices and broad target populations. The lowest value segment is local/sporadic vaccines, which account for less than 10% of value in all regions except the African Region (Fig. 5).

Vaccines are developed using a variety of technology platforms *(1)*. In 2021, when excluding COVID-19 vaccines, 60% of vaccines use traditional platforms while only 4% use innovative technologies. By contrast, 36% of COVID-19 vaccines use innovative technology platforms. This is an important technological shift that highlights the potential role those technologies may play in the rapid design and manufacture of future vaccines (see Annex 1 for details on the vaccines and platform definitions).

Fig. 5: Value by vaccine category and region, 2021 (excluding COVID-19)

Regional split of the total vaccine value between different vaccine category (total by region = 100%)

	WW Ped	LMIC Ped	HIC Ped	Children / adolescents	Local / sporadic	Adult
African Region	49%	16%	9%	10%	12%	3%
Region of the Americas	22%	0%	17%	19%	4%	38%
South-East Asian Region	31%	26%	1%	21%	6%	15%
European Region	15%	1%	22%	16%	5%	41%
Eastern Mediterranean Region	39%	10%	29%	8%	2%	12%
Western Pacific Region	27%	3%	16%	25%	10%	21%
Total	24%	3%	17%	19%	6%	32%

1. Vaccine platforms represent different ways of making and manufacturing a vaccine. In this report, vaccines are classified as follows: (a) toxoids, polysaccharide, live-viral and inactivated vaccines = traditional platforms group; (b) protein-based and conjugate vaccines = modern platforms group; (c) nucleic acid (e.g. mRNA) and viral vector vaccines = innovative platforms group.

Vaccine regulation

Vaccines are regulated by pharmaceutical medical product laws and are among the most complex medical products available. Regulators perform a set of regulatory functions spanning the medical product life cycle, from clinical trial oversight, product marketing authorization and registration, licensing establishments, regulatory inspections, testing products, post-marketing surveillance and vigilance activities. Stable, well-functioning and integrated regulatory systems with streamlined pathways and predictable timelines are key to facilitating timely access. However, inefficient regulatory systems can be a barrier to access to vaccines that are of assured quality. *(2)* Strengthening local vaccine production should be done in parallel with strengthening national regulatory capacity, as local production without quality assurance does not deliver public health benefits.

Flexibility and efficiency are two key principles of Good Regulatory Practices *(3)* that have been exercised by vaccine regulators in response to the need for timely and equitable access during the COVID-19 pandemic. This was evident by applying expedited pathways for the approval of COVID-19 vaccines through compassionate use, emergency use authorization, emergency use listing *(4)* (EUL), rolling submission and review processes. The EUL pathway involves a rigorous assessment of phase II and III clinical trial data as well as substantial data on safety, efficacy and manufacturing quality. These data are reviewed by independent experts who consider the body of evidence on the vaccine, the plans for monitoring its use and the plans for further studies. These efforts, supported by successful research and development, enabled regulators to grant authority for the use of COVID-19 vaccines within a record 11–18 months from WHO's declaration of the Public Health Emergency of International Concern (PHEIC). This was only possible by applying risk-based and reliance approaches (acceptance of assessments made by other national regulatory agencies) to assess the quality, safety and efficacy of the vaccines.

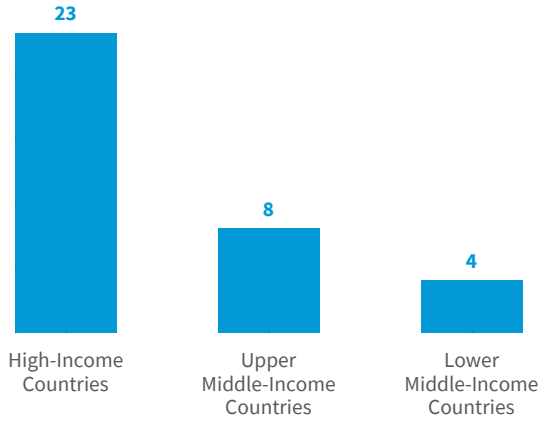
WHO continues to work with its Member States to strengthen their regulatory capacity and achieve stable, well-functioning and integrated regulatory systems. To provide strong regulatory oversight of vaccine development, manufacturing and deployment, the national regulatory authority should have reached a sufficient maturity level (ML 3) or be an advanced regulatory system (ML 4). As of December 2021, 35 vaccine-producing countries are considered by WHO to have reached at least level 3, two of which are new countries that have attained that designation since 2019 (Fig. 6).

2. Vaccines of assured quality include vaccines produced in a country with a stable, well-functioning and integrated national regulatory authority, including vaccines prequalified by WHO.
3. For more information refer to https://www.who.int/news/item/29-04-2021-who-publishes-new-guidance-to-promote-strong-efficient-and-sustainable-regulatory-systems.
4. The World Health Organization Emergency Use Listing Procedure is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of those products to people affected by a public health emergency.

In support of United Nations-based pooled procurement, 167 prequalified vaccines are available from 34 manufacturers. Between 2019 and 2021, 44% of the vaccine volume in this analysis was WHO prequalified. Since 2019, there has been an increase of 36 vaccines that are prequalified.

To decrease the burden of lengthy marketing authorization activities in multiple countries, 42 countries (21% of the total) now participate in the WHO collaborative registration procedure for vaccines. The procedure provides guarantees of high levels of quality assurance to countries and allows manufacturers to decrease the burden and cost of attaining marketing authorization in multiple countries. WHO, supported by UNICEF and other partners within the COVAX *(5)* facility, has assisted low- and middle-income country regulatory bodies to issue national authorizations of COVID-19 vaccines through various emergency use listing and collaborative registration procedures.

Fig. 6: ML 3/ML 4 vaccine-producing countries (N=35) according to World Bank income category



5. COVAX is the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator.

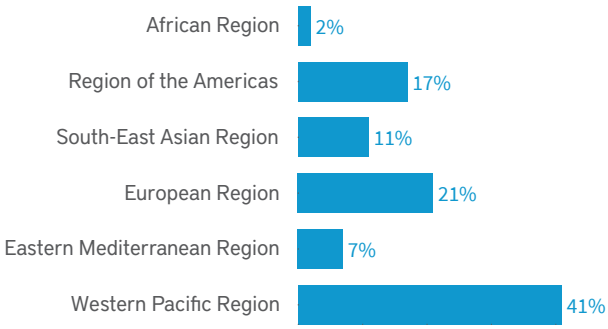
Manufacturing and supply

In 2021, 94 manufacturers were reported as distributing vaccines in WHO Member States. The entities include those performing all the steps of the vaccine manufacturing process, from producing the drug substance through to final packaging, as well as entities that perform only the final steps of filling and packaging before supply to the market. Geographically, in the Western Pacific and European regions have the largest number of manufacturers headquartered in their respective regions, with China (23) and India (7) as the top countries, representing 31% of all manufacturers (Fig. 7). Region of the Americas and European Region have the highest-value manufacturers when excluding COVID-19 vaccines. Four new manufacturers achieved WHO prequalification of at least one vaccine between 2019 and 2021.

In 2021, COVID-19 vaccines significantly changed the vaccine supply landscape. Various manufacturers emerged to capture global market value and volumes, with the top 10 manufacturers capturing almost 90% of the global value, indicating increased market concentration compared to all other vaccines (Fig. 8 and 9).

Excluding COVID-19 vaccines, the manufacturers that are capturing the largest share of the global market value and supplying the majority of volume are largely unchanged compared to 2019, with 10 manufacturers supplying 71% of the global volume. The Serum Institute of India (SII), the China National Biotechnology Group (CNBG), Sanofi, GSK, MSD and Pfizer are the only manufacturers in the top 10 for both value and volume

Fig. 7: Manufacturers by headquarter location, 2021



when excluding COVID-19 vaccines, similar to 2019. The global vaccine market therefore continues to be highly concentrated and reliant on a few manufacturers despite the new entrants during the COVID-19 pandemic (Fig. 10 and 11).

COVID-19 vaccines distributed in 2021 came from 19 manufacturers, 10 (52%) of which have no other marketed vaccine, and which collectively supplied 15% of the volume of COVID-19 vaccines. Only four COVID-19 vaccine manufacturers are in the top 10 in non-COVID-19 vaccine volumes, indicating that a significant portion of manufacturers of COVID-19 vaccines had limited prior experience in producing large volumes of vaccines (Fig. 12).

The number of technology platforms used by each manufacturer contributes to its relevance to the global supply. Eighty-six per cent of manufacturers use traditional platforms (55% only

Fig. 8: Top 10 manufacturers by value, 2021

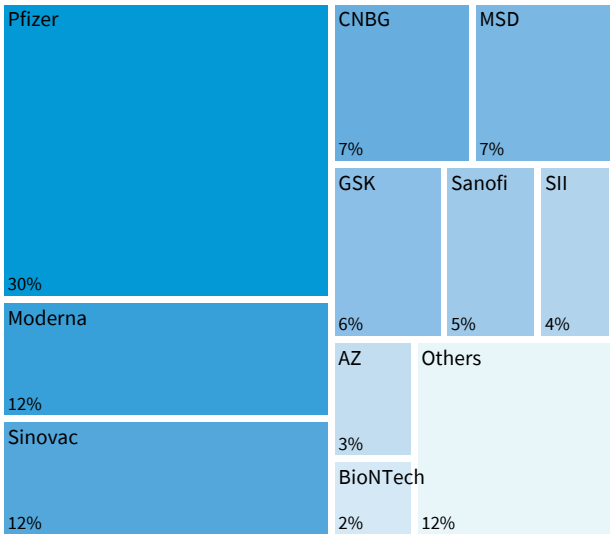


Fig. 9: Top 10 manufacturers by value (excluding COVID-19), 2021

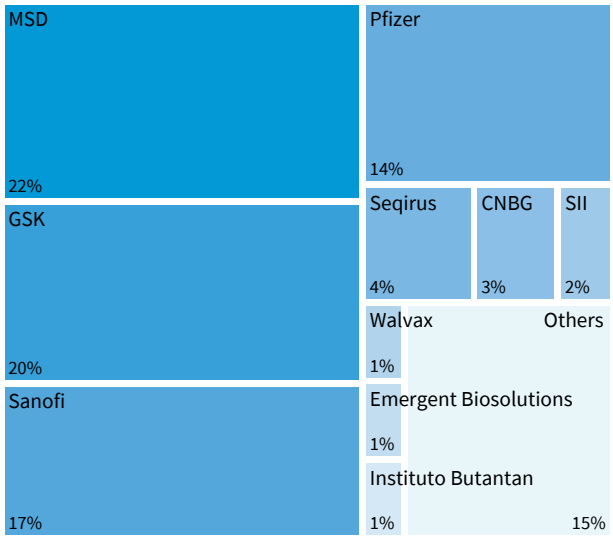


Fig. 10: Top 10 manufacturers by volume, 2021

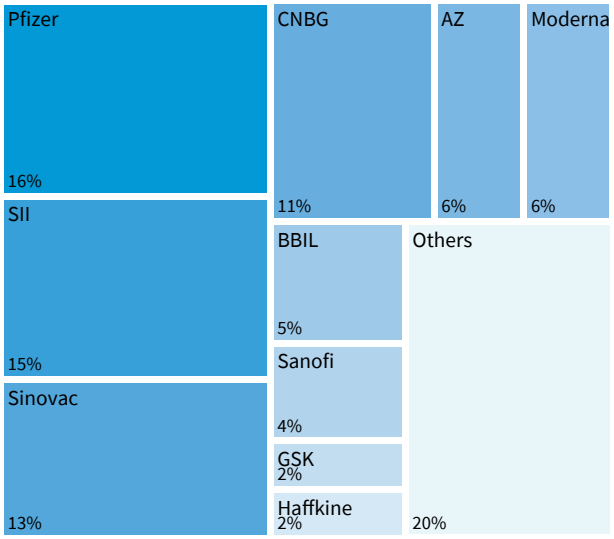
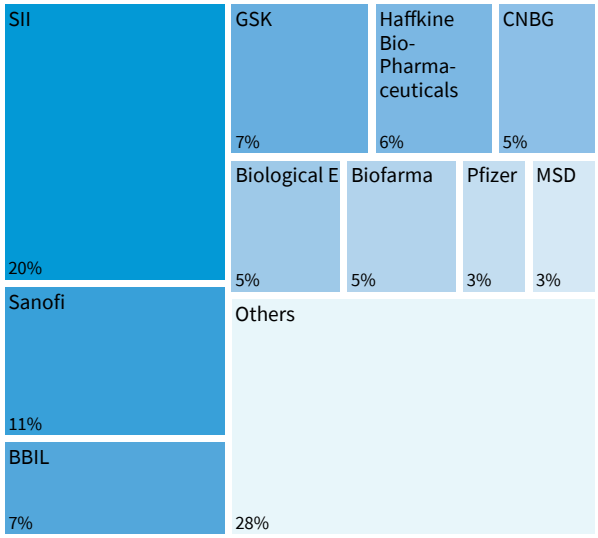


Fig. 11: Top 10 manufacturers by volume (excluding COVID-19), 2021

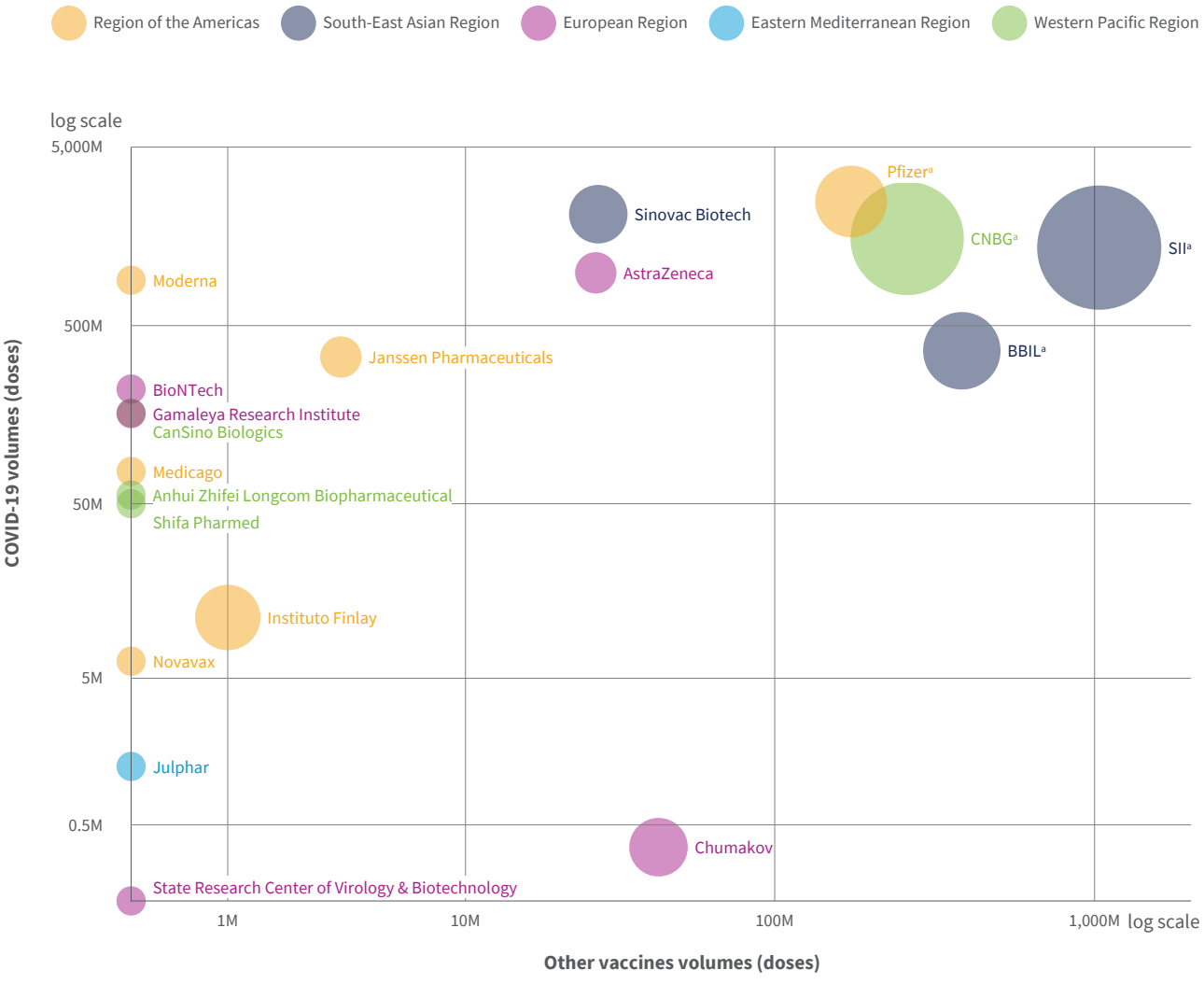


this platform), 38% modern platforms and 9% innovative platforms. Only four manufacturers (4%) also use innovative platforms in addition to the others and hence have the maximum flexibility for expanding supply and their portfolio. All manufacturers deploying innovative technologies are headquartered in the Region of the Americas or European Region, with the exception of SII, which is located in South-East Asia Region.

Only six of the 94 manufacturers produce more than eight vaccines and distribute globally. Fifteen manufacturers are medium-sized, with four to eight vaccines and sales outside of their region; 49 are small, with three or fewer vaccines and sales within their region only. The global vaccine market is highly dependent on only nine manufacturers (10% of the total number of manufacturers) that have more than five vaccines and distribute vaccines globally and across multiple technology platforms. Together, those

Fig. 12: COVID-19 manufacturers – comparison of COVID-19 and non COVID-19 volumes

Size of the bubble indicates the number of vaccines produced by the manufacturer.

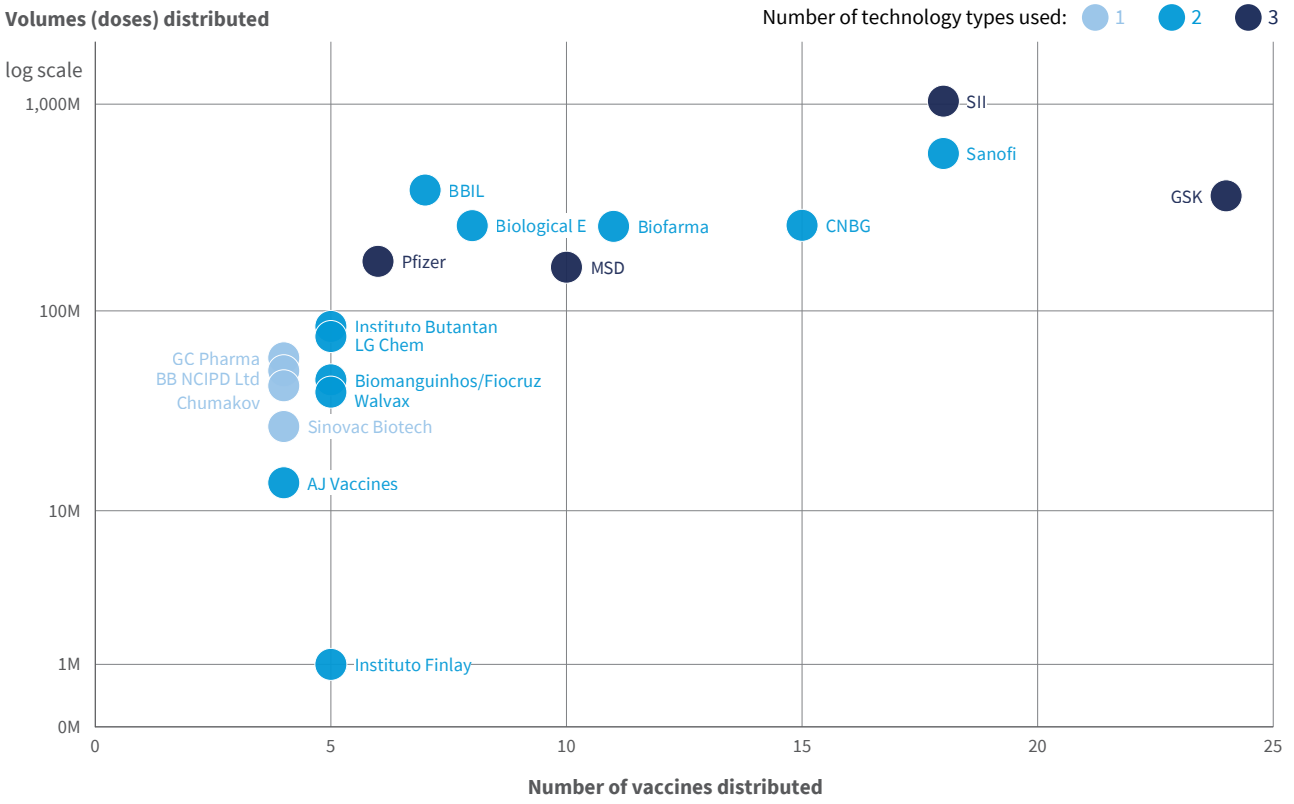


[a] indicates inclusion in the top 10 manufacturers by volume excluding COVID-19

manufacturers provide 64% of global supply in 2021, excluding COVID-19 vaccines (Fig. 13). Of those manufacturers, four are located in India (South-East Asia Region), two are located in the Region of the Americas and the European Region and one is located in Western Pacific Region.

Technology transfers and partnerships across the manufacturing process can influence the flexibility and scalability of supply, and have increased with the advent of COVID-19 vaccines. For example, several manufacturers do not perform all manufacturing steps and instead depend on receiving bulk vaccine from another manufacturer that they fill into vials and package for distribution. The intent, scope, extent and reach of such collaborations are evolving quickly, and are important in assessing the full extent of the dependence on a few manufacturers. Given the growing importance of this trend, a deeper understanding of such network dynamics is needed and is a limitation of this analysis.

Fig. 13: Manufacturers by volume, portfolio size and number of technology types used (excluding COVID-19)



Global distribution

Lack of equity in access to COVID-19 vaccines, particularly in African Region and Eastern Mediterranean Region, is especially problematic. Countries and regions with more ready financial resources (the United States and Europe) and with local manufacturers (China and India) were able to quickly secure supplies of the limited COVID-19 vaccines available. These dynamics are seen for other vaccines, but for COVID-19 vaccines were particularly accentuated, as shown in Fig. 14.

Among vaccines that could potentially be used worldwide, access in lower-income settings has considerably improved over time, but remains limited, particularly for human papillomavirus (HPV) vaccines and, to a lesser extent, also for PCV (Fig. 15). Compared to 2019, those access issues remain unchanged.

Whereas many HICs use vaccines for adults as well as children, lower-income countries do not extend vaccination across the life course (Fig. 16). Adult vaccines account for less than 10% of doses of vaccines used in low-income countries (LICs). Eighty-six per cent of HICs report having a seasonal influenza vaccine compared to 71% of upper-middle-income countries (UMICs), 41% of lower middle-income countries (LMICs) and none of LICs (Fig. 17). The costs to countries of adult vaccines in HICs is 40% of the total vaccine cost, almost equivalent to the value of paediatric vaccines (Fig. 5). Extending life-course vaccination in LICs will likely require a considerable increase in immunization budgets.

Fig. 14: Comparison of volume of COVID-19 vaccine and all other vaccines used, 2021

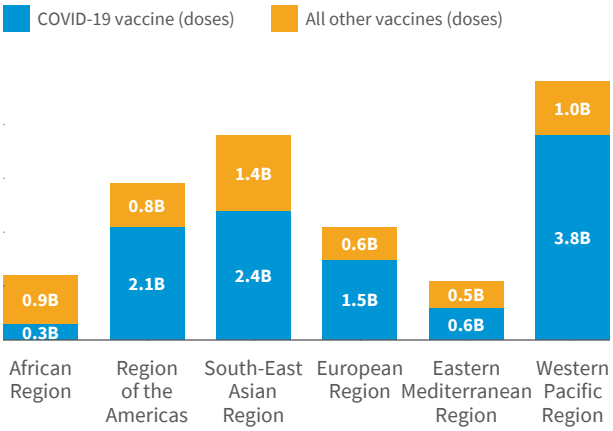
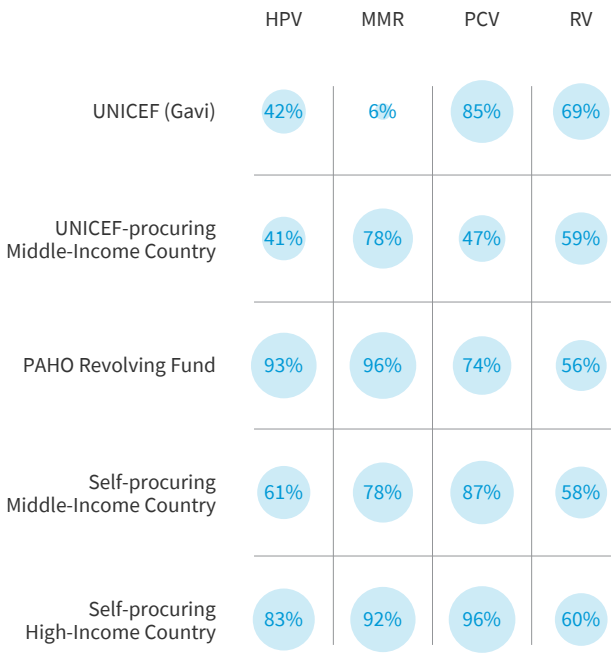


Fig. 15: Per cent of countries using select vaccines by procurement mechanism, 2021



National stock-outs *(6)* of one or more vaccines were reported by 60 countries in 2021, 43% of which were in the African Region, with a trend consistent with previous years. Global vaccine shortage was indicated as the cause of a national stock-out by at least one country for only nine vaccines.

The known global shortage of HPV vaccine may have contributed to reported stock-outs, but it is more likely to be a cause for the delayed introduction of HPV vaccination in LICs and LMICs. There is no evidence that the COVID-19 pandemic changed patterns of reported stock-outs caused by vaccine shortages or quality issues (Fig. 18).

6. From the 2014 Global Vaccine Action Plan: "A stock-out event is defined when a stock-out of a vaccine occurred for a duration of at least one month."

Fig. 16: Proportion of doses of vaccines used in each income group that are classified as Adult, 2021

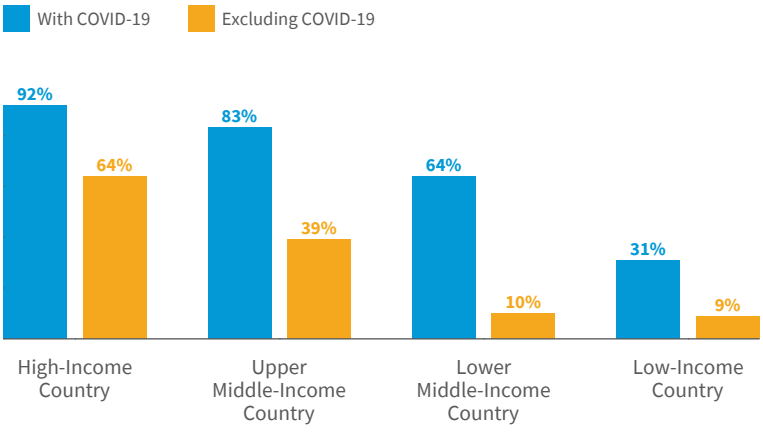


Fig. 17: Per cent of countries where influenza vaccine was distributed, 2021

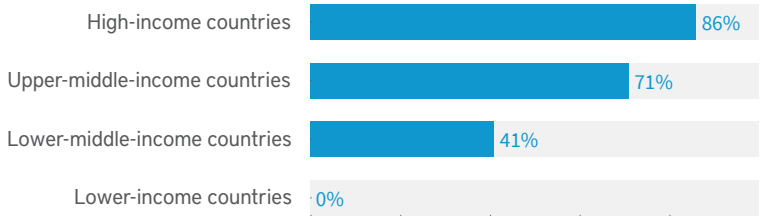
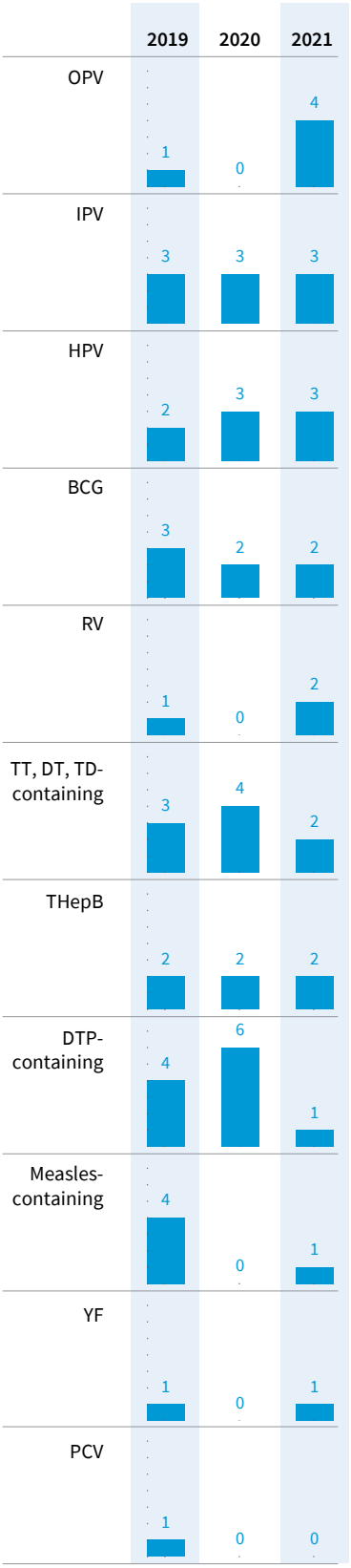


Fig. 18: Number of stock-outs caused by vaccine shortage or a quality issue



Market health and regional supply security

The health of the vaccine market *(7)* depends, among other things, on the balance of supply and demand, the number of countries using a vaccine, the variability from year to year in procured vaccine dose volumes, the number of manufacturers, the number of prequalified *(8)* vaccines and the degree of concentration in the available supply. Table 1 describes different vaccine markets along key characteristics. The depicted vaccines markets are among the top 10 in volume in at least one income group. The ones deemed to be at risk are highlighted based on the number of prequalified vaccines, the share of volumes by manufacturers and the volume change. The characteristics of market health for specific vaccine segments may differ from the global picture.

The vaccine markets that display poor health are either relatively new or very mature, suggesting that vaccines at both extremes of the vaccine life cycle are more likely to have poor market health.

The health of markets for vaccines that are used to respond to emergency outbreaks should be viewed individually, since the risk of a surge in demand is high, and the size of the need highly variable; furthermore, under normal circumstances fewer than 100 million doses of the vaccines are procured annually (Table 2). The risk of surges in demand, the low number of manufacturers and of prequalified vaccines and the low predictable commercial value leaves six of the eight vaccines with a higher risk of supply constraints. Furthermore, only four of those vaccines have established stockpiles intended to meet urgent demand, and only one vaccine uses innovative technology that could improve the ability to meet surges in demand.

7. This analysis is consistent with, but not intended to replicate, the concepts of the Gavi Healthy Market Framework, which can be accessed at: Market Shaping (gavi.org).

8. WHO prequalification of medicines is a service provided by WHO to assess the quality, safety and efficacy of medicinal products. Prequalification is important to the primarily lower-income countries that purchase vaccines through United Nations pooled procurement mechanisms and where procurement of non-prequalified vaccines is limited.

In some regions, vaccines are almost completely supplied by manufacturers headquartered outside the region; this condition can be highly problematic, especially in the event of emergencies and outbreaks. Vaccines in the African and Eastern Mediterranean regions are, respectively, supplied 99% and 94% by manufacturers head- quartered in other regions. By contrast, the South-East Asian and Western Pacific regions use the highest percentage of vaccines sourced from within the same region, at 79% and 78%, respectively, due to the presence of suppliers

Table 1: Market characteristics for the top 20 most widely used vaccines

Poor market health

Vaccine	# of countries and territories	2019-2021 volume change	# of manufacturers	# of prequalified or emergency use listing vaccines	Concentration (% of volume share of top 2 vaccines)
BCG	163	0%	14	4	61%
PCV	161	1%	6	4	80%
COVID-19	157	100%	19	10	42%
Td containing	155	-14%	15	5	74%
HepB	147	4%	17	4	42%
IPV	143	15%	11	6	69%
DTwP primary	124	18%	9	6	53%
HPV	121	22%	5	3	85%
RV	120	12%	5	4	63%
MMR	119	-19%	6	3	70%
Seasonal Influenza	115	29%	39	9	40%
OPV[a]	98	-40%	10	7	65%
YF[a]	75	-23%	5	4	77%
DTaP primary	69	-2%	2	1	100%
TdaP containing	62	-5%	4	0	93%
MR	58	-80%	6	2	90%
Varicella	57	-12%	8	2	78%
Rabies	36	-22%	13	3	73%
Measles[a]	27	-40%	5	2	93%
Shingles	9	-1%	1	0	100%

[a] Yellow Fever (YF), Oral Polio Vaccine (OPV) and Measles could alternatively be grouped under the emergency antigens. The associated figures capture both the routine and emergency market characteristics.

Table 2: Market characteristics for vaccines that could be needed in an emergency, 2021

Poor market health

Vaccine	# of countries	2019-2021 volume change	# of manufacturers	# prequalified vaccines	Concentration (% of volume share of top vaccine)	Stockpile
Cholera	15	-2%	3	3	64%	Yes
TCV	4	53%	1	1	100%	No
JE	20	-2%	11	3	37%	No
MenA conj.	13	-130%	1	1	100%	Yes
MenAC conj.	2	78%	3	0	62%	No
MenACYW-135 conj.	50	-34%	3	3	51%	No
Smallpox/Monkeypox	1	6%	2	0	67%	Yes
Ebola	0	100%	1	1	100%	Yes

Fig. 19: Regional vaccine volume distribution versus supply

With COVID-19

Supplier:	Distributed in: African Region	Region of the Americas	South-East Asian Region	European Region	Eastern Mediterranean Region	Western Pacific Region
African Region	0%	0%	0%	0%	0%	0%
Region of the Americas	17%	57%	6%	56%	26%	15%
South-East Asian Region	43%	6%	79%	2%	27%	1%
European Region	25%	29%	2%	39%	23%	6%
Eastern Mediterranean Region	0%	0%	0%	0%	6%	0%
Western Pacific Region	14%	8%	13%	4%	17%	78%
TOTAL	100%	100%	100%	100%	100%	100%

Without COVID-19

Supplier:	Distributed in: African Region	Region of the Americas	South-East Asian Region	European Region	Eastern Mediterranean Region	Western Pacific Region
African Region	1%	0%	0%	0%	0%	0%
Region of the Americas	7%	31%	1%	11%	9%	5%
South-East Asian Region	57%	21%	93%	6%	56%	5%
European Region	26%	39%	3%	76%	26%	5%
Eastern Mediterranean Region	0%	0%	0%	0%	4%	0%
Western Pacific Region	9%	8%	3%	7%	4%	85%
TOTAL	100%	100%	100%	100%	100%	100%

in India (South-East Asia Region) and China (Western Pacific Region) (Fig. 19). Compared to all other vaccines, all regions relied more on Region of the Americas and Western Pacific Region for the supply of COVID-19 vaccine (Fig. 20). South-East Asia Region was not an important source of COVID-19 vaccines outside its region, whereas the South-East Asia Region is a majority supplier for all other vaccines in the African and Eastern Mediterranean regions (Fig. 19).

In the African and Eastern Mediterranean regions, more than 90% of COVID-19 vaccines were sourced from outside the regions (Fig. 20) – those two regions also had the most limited access to COVID-19 vaccines, receiving only 3% and 6% of the total distributed vaccines in 2021. In response to the delayed distribution of COVID-19 vaccines in the African Region, the African Union set a goal of increasing the availability and use of vaccines produced within the region and wishes to expand beyond initial plans for the manufacturing of COVID-19 vaccines.

Fig. 20: Source of COVID-19 vaccine volumes by WHO region

	Distributed in:					
Supplier:	African Region	Region of the Americas	South-East Asian Region	European Region	Eastern Mediterranean Region	Western Pacific Region
African Region	0%	0%	0%	0%	0%	0%
Region of the Americas	45%	67%	9%	74%	41%	17%
South-East Asian Region	2%	0%	71%	0%	2%	0%
European Region	23%	26%	2%	23%	21%	6%
Eastern Mediterranean Region	0%	0%	0%	0%	8%	0%
Western Pacific Region	30%	7%	19%	2%	28%	77%
TOTAL	100%	100%	100%	100%	100%	100%

Pricing and procurement

Vaccine pricing depends on multiple factors, including the type of vaccine, the income group of the procuring country, the procurement mechanism and the contract terms.

Vaccines are primarily self-procured by countries. Self-procuring MICs, many of which face challenging fiscal environments, account for 59% of volume (39% for India and China; 20% for 71 other self-procuring MICs) (Fig. 21). Changes from 2019 are due to COVID-19 vaccines, which are primarily self-procured, with 90% of all doses in 2021 going to self-procuring MICs and HICs and only 10% of COVID-19 vaccines through pooled mechanisms.

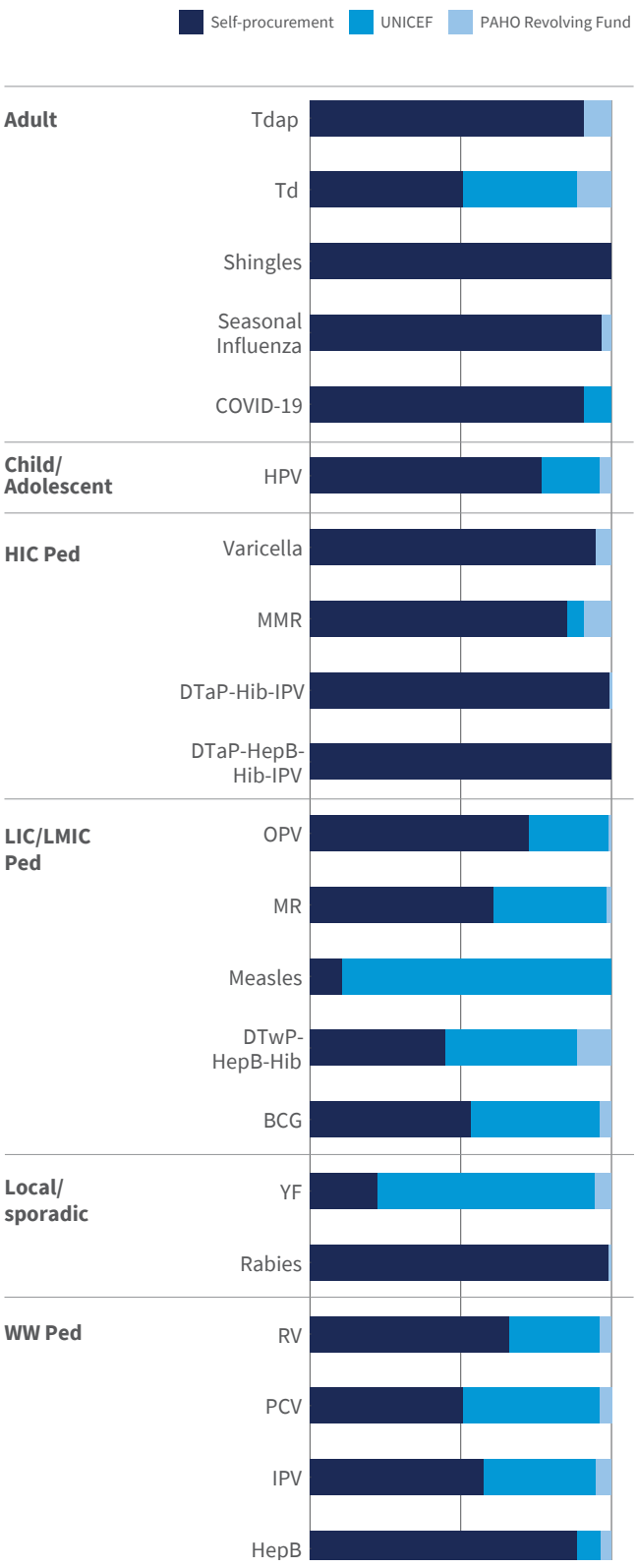
The pooled procurement mechanisms of UNICEF and the Pan American Health Organization Revolving Fund (PAHO RF) play an important role in procuring vaccines for lower-income settings. While UNICEF procures primarily for low- and lower-middle-income countries, PAHO RF procures primarily for UMICs.

United Nations procurement mechanisms represented 15% of the volume and 7% of the value of vaccines in 2021. Excluding COVID-19 vaccines, the pooled procurement mechanisms account for 30% of total volume and 5% of total value (Fig. 21). As Fig. 22 illustrates, pooled procurement mechanisms are primarily used for paediatric vaccines, especially in LMICs. Twenty-six manufacturers provided vaccines to at least one pooled procurement mechanism in 2021. Of these, four manufacturers provided most of the volume (SII, Pfizer, AstraZeneca, Sinovac Biotech).

Fig. 21: Volume and value by procurement mechanism, 2021

	VOLUME		VALUE	
	With COVID-19	Excluding COVID-19	With COVID-19	Excluding COVID-19
UNICEF (Gavi)	11%	23%	3%	3%
UNICEF-procuring Middle-Income Country	3%	1%	3%	0%
PAHO Revolving Fund	1%	4%	0%	2%
Self-procuring Middle-Income Country	59%	54%	39%	27%
Self-procuring High-Income Country	25%	18%	54%	68%

Fig. 22: Pooled versus self-procurement analysis, 2021



Pooled procurement mechanisms actively shape markets to improve the availability and affordability of quality assured vaccines. In the 2019 Global Vaccine Market Report, procurement through pooled procurement mechanisms was associated with lower prices, an observation verified in 2021, where we see similar dynamics, as shown in Table 3. Nevertheless, for some LMIC paediatric vaccines, the effect is diminished, as large self-procuring countries attain lower prices, supporting the 2019 conclusions on the impact of volume on price for self-procuring countries.

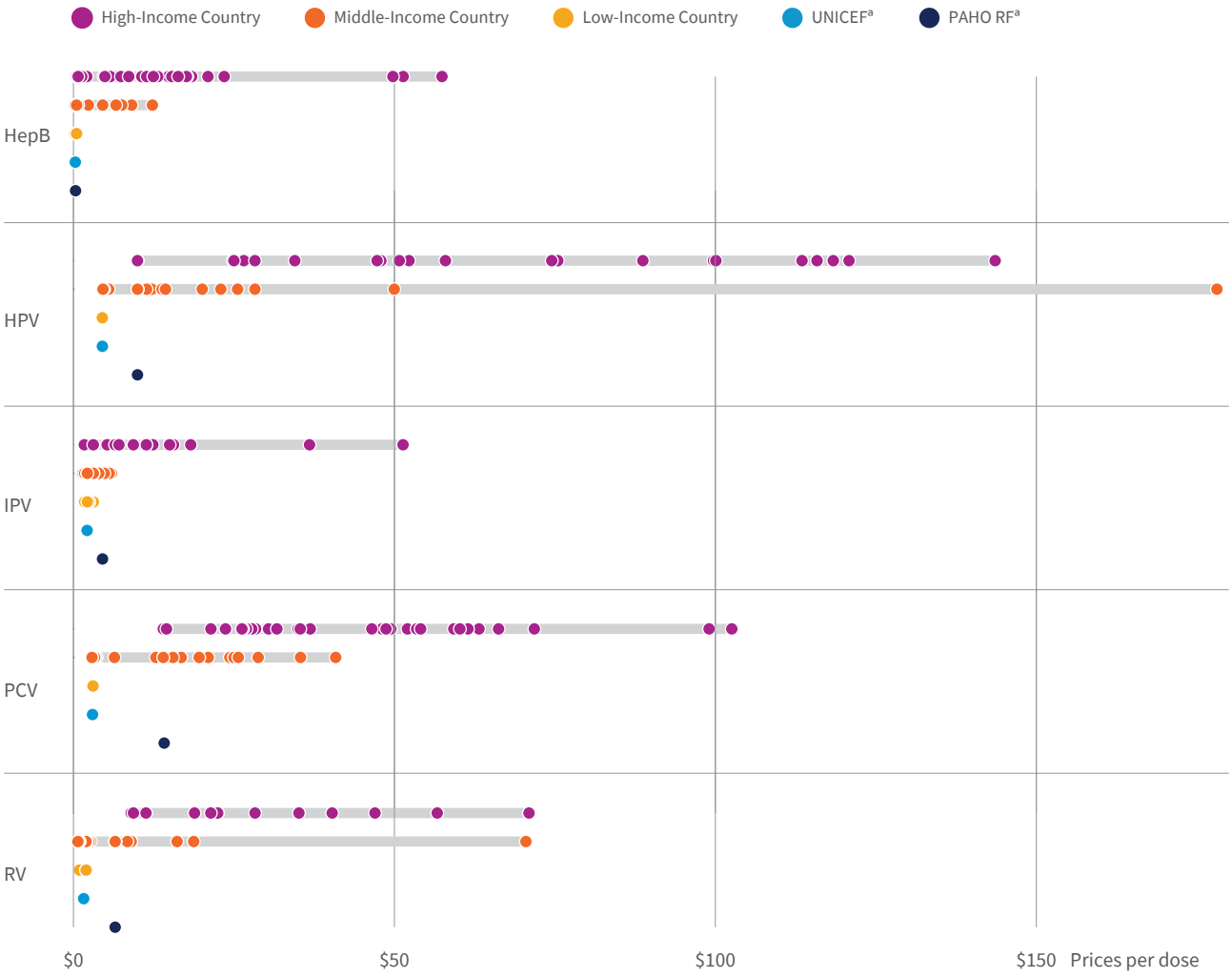
Fig. 23 also shows that the prices of paediatric vaccines of worldwide use are tiered by country income level. In descending order, the largest price variances were noted for Td (Adult), HepB (WW Ped), HPV (Children/Adolescents), YF (Local/Sporadic) and measles (LIC/LMIC Ped) (Fig. 23). However, there is still opportunity for streamlining. Tiered pricing by income group across all procurement mechanisms (Fig. 24) shows wide price ranges for the same vaccine and price overlaps between MICs and HICs. Vaccines earlier in their life cycle and with relatively few manufacturers (HPV, PCV, RV) have the largest price differential across income groups.

Fig. 23: Price differences across income groups, relative to lowest price, 2021

Proportion of WAP in each income group compared to the lowest WAP amongst the 4 income groups

	Lower-Income Country	Lower Middle-Income Country	Upper Middle-Income Country	High-Income Country
Tdap	–	Lowest price	1.03	2.10
Td	Lowest price	1.02	2.07	60.18
Shingles	–	–	–	–
Seasonal Influenza	–	1.03	Lowest price	2.39
COVID-19	Lowest price	1.21	1.54	1.84
HPV	Lowest price—	1.18	3.13	14.92
Varicella	–	–	Lowest price	1.57
MMR	Lowest price	1.53	2.82	4.51
DTaP-Hib-IPV	–	–	Lowest price	1.64
DTaP-HepB-Hib-IPV	–	–	Lowest price	1.32
OPV	1.30	Lowest price	2.80	2.24
MR	Lowest price	1.21	1.20	–
Measles	Lowest price	1.05	2.61	13.59
DTwP-HepB-Hib	1.07	Lowest price	1.31	7.32
BCG	Lowest price	1.65	2.52	6.72
YF	Lowest price	1.16	1.31	13.69
Rabies	–	1.03	Lowest price	1.25
RV	1.31	Lowest price	5.84	9.91
PCV	Lowest price	1.20	6.05	10.30
IPV	Lowest price	1.08	2.46	3.59
HepB	Lowest price	3.23	2.77	26.83

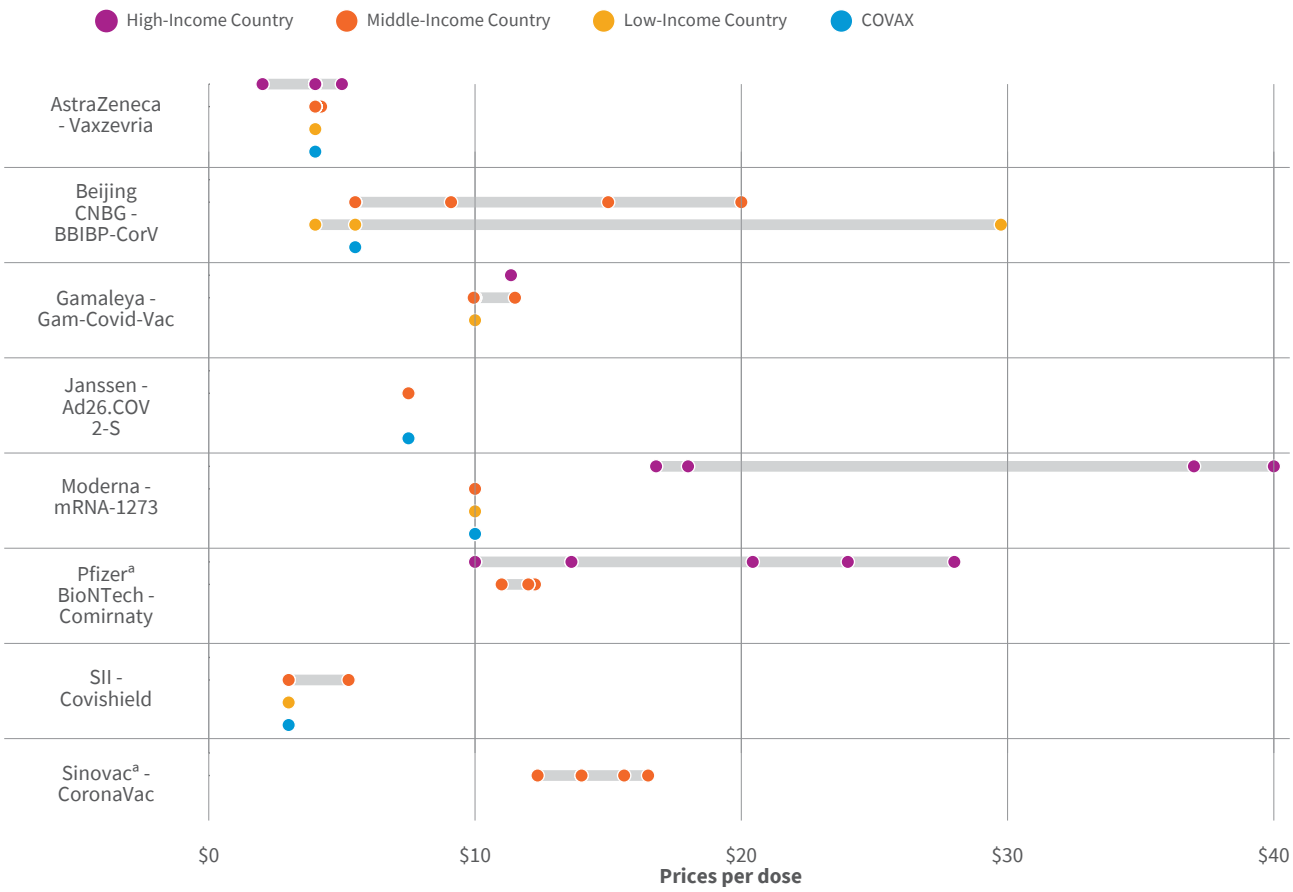
Fig. 24: Worldwide paediatric vaccine prices (USD per dose) tiering by income level, 2021



[a] indicates the WAP shown in Table 3

For COVID-19 vaccines, the impact of pooled procurement was, in almost all cases, a contractual guarantee of the lowest price for the purchasing country. Limited reported data on COVID-19 prices suggest that tiering was not as pronounced– whereas average HPV and PCV vaccines have an approximately 18-fold difference between high and low prices, COVID-19 prices varied by only three-fold (Table 3). Large public investments in vaccine development for some manufacturers in HICs was reflected in lower HIC prices. Prices for several vaccines demonstrated considerable price overlap within and across income groups.

Fig. 25: COVID-19 vaccine prices by income level, 2021



All prices shown are those reported by countries except COVAX prices which are those listed by UNICEF

[a] These suppliers have not agreed to the publication and prices are not shown

Price changes from 2019 to 2021 for the 20 most commonly used vaccines across income groups by type of procurement method do not show a clear trend (Table 3). Larger variability was observed for self-procuring HICs, where the average change in median price was 35%, ranging from -7% for OPV to 121% for YF vaccine. In this self-procuring group, the median prices of HPV, RV and PCV vaccines rose by 63%, 55% and 43%, respectively, from 2019 to 2021. Across all income groups and procurement methods there was an average price increase of 17% for the vaccines in Table 3 (not adjusting for inflation) between 2019 and 2021.

YF vaccine is primarily procured through pooled mechanisms and has experienced price increases of 22% by UNICEF and 42% by PAHO RF procurement since 2019, which is attributed to the low starting prices combined with reliance on a few dominant manufacturers.

Table 3: Median prices (USD per dose) by procurement mechanism, 2019–2020

Weighted average price for UNICEF and PAHO RF

	UNICEF			UNICEF Middle-Income Countries			PAHO Revolving Fund			Self-procuring Middle-Income Countries			Self-procuring High-Income Countries		
	2019	2020	2021	2019	2020	2021	2019	2020	2021	2019	2020	2021	2019	2020	2021
BCG	$0.13	$0.16	$0.14	$0.14	$0.22	$0.25	$0.22	$0.23	$0.33	$0.25	$0.19	$0.18	$1.03	$2.03	$1.75
DTaP-HepB-Hib-IPV							$21.12	$21.12	$21.12	$22.44	$28.55	$27.43	$31.35	$39.01	$35.13
DTaP-Hib-IPV							$14.80	$15.84	$16.31	$17.22	$18.59	$21.29	$20.69	$21.90	$24.34
DTwP-HepB-Hib	$0.88	$1.15	$0.90	$0.80	$0.86	$0.89	$1.09	$1.01	$1.03	$1.26	$1.28	$1.34	$4.92	$3.92	$4.66
HepB	$0.28	$0.24	$0.29	$0.29	$0.34	$0.42	$0.31	$0.43	$0.43	$1.26	$1.07	$1.24	$6.69	$11.07	$12.28
HPV	$4.51	$4.54	$4.51	$4.85	$14.27	$14.51	$9.45	$9.98	$9.98	$12.71	$13.17	$20.06	$50.06	$57.12	$81.61
IPV	$2.30	$2.18	$2.13	$2.62	$2.26	$2.17	$5.53	$4.58	$4.53	$4.48	$3.83	$4.25	$9.50	$7.36	$11.86
Measles	$0.32	$0.32	$0.33	$0.32	$0.32	$0.35				$0.73	$0.60	$0.60			
MMR	$2.50	$2.26	$1.42	$1.81	$2.48	$2.99	$3.31	$4.43	$3.82	$3.96	$4.00	$5.35	$6.93	$7.49	$7.81
MR	$0.66	$0.65	$0.72	$0.66	$0.98	$0.80	$0.91	$1.63	$1.49	$1.12	$0.73	$0.78			
OPV	$0.14	$0.14	$0.14	$0.16	$0.17	$0.21	$0.16	$0.14	$0.13	$0.21	$0.18	$0.15	$0.27	$0.36	$0.25
PCV	$2.99	$2.95	$2.97	$11.96	$15.18	$15.92	$13.74	$14.22	$14.14	$18.74	$19.61	$21.00	$30.15	$45.49	$43.21
Rabies							$13.00	$9.92	$10.44	$8.07	$17.03	$8.96	$21.14	$31.96	$36.55
Rota	$2.04	$1.72	$1.60	$1.77	$2.65	$2.12	$6.50	$6.50	$6.50	$7.28	$6.25	$12.28	$14.55	$21.00	$22.48
Flu		$3.75	$4.35		$3.30	$5.10	$4.05	$2.93	$3.24	$3.87	$3.40	$3.89	$6.28	$7.60	$8.21
Shingles													$100.11	$108.23	$102.00
Td	$0.12	$0.16	$0.11	$0.12	$0.15	$0.14	$0.10	$0.10	$0.10	$0.27	$0.22	$0.22	$7.05	$10.73	$7.20
Tdap							$12.72	$12.94	$12.77	$21.54	$15.13	$15.95	$14.78	$17.33	$15.97
Varicella							$16.59	$15.85	$13.81				$25.35	$35.67	$32.80
YF	$1.15	$1.03	$1.22	$1.03	$1.44	$1.46	$1.48	$1.39	$1.38	$19.10	$23.79	$20.64	$20.05	$47.67	$44.28
COVID-19			$5.75			$5.58						$10.66			$14.66

Low High

The median prices stated in the table are taken across products for the same antigen. The data used for the median calculation are reported by countries, might contain errors, and the reporting countries are solely responsible for their accuracy.

Section 3

Annexes

Annex 1: Data sources and definitions

Primary data

The WHO/UNICEF Joint Reporting Form purchase data reported by countries provides the primary data source for this report: WHO Immunization Data portal.

World Bank gross national income (GNI) per capita data are used for determining the country income level: GNI, Atlas method (current US$) | Data (worldbank.org).

Gavi, the Vaccine Alliance, eligibility criteria are used for determining the 2021 status of each country: Eligibility (gavi.org).

Secondary/supplementary data

The Global Vaccine Market Model (GVMM) has been used to supplement historical volumes information where not reported elsewhere. The GVMM estimates demand by country and for 60 vaccines across all WHO Member States, leveraging publicly available information: Global Vaccine Market Model.

PAHO RF pricing information is used to supplement price information where not reported: PAHO Revolving Fund Vaccine Prices for 2021 – PAHO/WHO | Pan American Health Organization.

UNICEF Supply Division pricing information is used to supplement price information where not reported: Vaccines pricing data | UNICEF Supply Division. UNICEF Supply Division volume information was used to reference volume information: Pricing data | UNICEF Supply Division; Gavi shipment reports | UNICEF Supply Division.

Evaluate data were used to supplement the market values for a subset of vaccines: Evaluate Pharma | Evaluate.

Publicly reported sales from individual manufacturers were referenced to supplement the market values for a subset of vaccines.

Vaccines included in the report according to primary use

This is **not** an exhaustive list of all vaccines available worldwide; these are the vaccines (47) and manufacturers (94) for which distribution during 2021 is reported.

ABBREVIATION OF THE VACCINE USED IN THE REPORT	NUMBER OF COUNTRIES IDENTIFIED AS USING VACCINE DURING 2021				VACCINE MANUFACTURERS SUPPLYING MARKET IN 2021		LONG NAME OF VACCINE OR GROUPING
	LIC (29)	LMIC (54)	UMIC (56)	HIC (64)	# OF MANUFACTURERS	# OF WHO PREQUALIFIED VACCINES	
WORLDWIDE PAEDIATRIC (WW PED) VACCINES							
HepB	6	41	52	48	17	4	Hepatitis B
Hib	0	4	10	21	8	3	Haemophilus influenzae type B
IPV	28	52	32	31	11	6	Inactivated polio
PCV	22	41	41	57	6	4	Pneumococcal conjugate
RV	21	34	30	35	5	4	Rotavirus
LOW- AND MIDDLE-INCOME COUNTRY PAEDIATRIC (LMIC PED) VACCINES							
BCG	28	52	49	34	14	4	Bacillus Calmette-Guérin (for tuberculosis)
DT	2	16	23	12	13	3	Diphtheria and tetanus
DTwP	3	23	30	12	10	3	Diphtheria, tetanus and whole cell pertussis
DTwP primary	28	50	33	13	9	6	DTwP-HepB-Hib (penta); DTwP-HepB-Hib-IPV (hexa)
Hib-MenAC PS	0	0	1	1	1	0	Hib combined with meningococcal A polysaccharide
Malaria	1	1	0	0	1	1	Malaria
Measles	14	6	6	1	5	2	Measles monovalent
MenA conj.	10	3	0	0	1	1	Meningococcal A conjugate
MenAC conj.	0	0	1	1	3	0	Meningococcal A and C conjugate
Men AC PS	0	1	1	0	2	0	Meningococcal A and C polysaccharide
MR	13	31	13	1	6	2	Measles and rubella
OPV	23	40	25	10	10	7	Oral polio
TCV	1	2	1	0	1	1	Typhoid conjugate
Typhoid PS	0	2	11	18	7	1	Typhoid polysaccharide
HIGH-INCOME COUNTRY PAEDIATRIC (HIC PED) VACCINES							
DTaP primary	0	1	21	47	2	1	DTaP-HepB-IPV (penta); DTaP-HepB-Hib-IPV (hexa)
DTaP boosters	0	0	18	43	7	2	DTaP; DTaP-IPV
HepA	0	3	13	24	8	2	Hepatitis A

ABBREVIATION OF THE VACCINE USED IN THE REPORT	NUMBER OF COUNTRIES IDENTIFIED AS USING VACCINE DURING 2021				VACCINE MANUFACTURERS SUPPLYING MARKET IN 2021		LONG NAME OF VACCINE OR GROUPING
	LIC (29)	LMIC (54)	UMIC (56)	HIC (64)	# OF MANUFACTURERS	# OF WHO PREQUALIFIED VACCINES	
MMR	1	19	42	57	6	3	Measles, mumps, rubella
MMRV	0	0	1	9	3	0	Measles, mumps, rubella, varicella
Varicella	0	1	17	39	8	2	Varicella
CHILDREN/ADOLESCENTS							
HPV	9	23	37	52	5	3	Human papillomavirus
MenACYW-135 conj.	0	3	17	30	3	3	Meningococcal A, C, Y, W conjugate
MenB	0	0	0	18	2	0	Meningococcal B
MenC conj.	0	0	1	16	3	0	Meningococcal C conjugate
ADULT							
COVID-19	26	49	38	44	19	0	COVID-19 or SARS-CoV-2
HepA+B	0	0	0	5	1	0	Hepatitis A and B combined
PPV23	0	2	13	40	3	0	Pneumococcal polysaccharide
Seasonal influenza	0	22	39	54	29	9	Seasonal influenza
Shingles	0	0	0	9	1	0	Varicella zoster
Td containing	26	52	45	32	15	5	Tetanus, diphtheria (reduced antigen content)
TdaP containing	0	2	13	47	4	0	Tetanus, diphtheria, acellular pertussis
TT	0	3	7	8	9	5	Tetanus toxoid
LOCAL/SPORADIC							
Anthrax	0	0	1	1	2	0	Anthrax
Cholera	8	6	0	1	3	3	Cholera
Ebola	0	0	0	0	1	1	Ebola
EV71	0	0	1	0	2	0	Enterovirus 71
JE	0	9	3	8	11	3	Japanese encephalitis
MenACYW-135 PS	0	2	3	2	5	0	Meningococcal A, C, Y W polysaccharide
Rabies	0	8	13	15	13	3	Rabies
Smallpox/monkeypox	0	0	0	1	2	0	Smallpox/monkeypox
TBE	0	1	3	2	4	0	Tick-borne encephalitis
YF	17	20	21	17	5	4	Yellow fever

Manufacturer and vaccine technology categories

Criteria for determining manufacturer category

Manufacturer size

SMALL	MEDIUM	LARGE
Produce less than four vaccines	Produce between four and eight vaccines	Produce more than eight vaccines

Manufacturer distribution

LOCAL	GLOBAL
Manufacturer sells vaccines in less than two WHO regions	Manufacturer sells vaccines in two or more WHO regions

Vaccines within each technology category

TRADITIONAL		
Anthrax	JE	RV
BCG	Measles	Seasonal influenza
Cholera	MenAC PS	Smallpox/monkeypox
COVID-19	MenACYW-135 PS	TBE
DT	MMR	Td containing
DTwP	MMRV	TT
DTwP primary	MR	Typhoid PS
EV71	OPV	Varicella
HepA	PPV23	YF
IPV	Rabies	

MODERN		
Anthrax	HepE	MenACYWX conj.
COVID-19	Hib	MenC conj.
DTaP boosters	Hib-MenAC PS	PCV
DTaP primary	HPV	Seasonal influenza
DTaP-HepB-Hib	JE	Shingles
DTaP-HepB-Hib-IPV	Malaria	TCV
DTwP-HepB-Hib	MenA conj.	TdaP containing
DTwP-HepB-Hib-IPV	MenAC conj.	
HepA+B	MenAC-Hib conj.	
HepB	MenACYW-135 conj.	

INNOVATIVE			
COVID-19	Dengue	Ebola	MenB

Annex 2: Additional resources

UNICEF Immunization Supplies and Logistics: Influencing markets | UNICEF Supply Division.

PAHO Revolving Fund: PAHO Revolving Fund - PAHO/WHO | Pan American Health Organization.

Gavi, the Vaccine Alliance, vaccine road map public summaries and other supply- and procurement-related documents: Market Shaping (gavi.org).

WHO MI4A vaccine purchase data (in Excel format for download) and vaccine-specific global market studies: Immunization, Vaccines and Biologicals (who.int).

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