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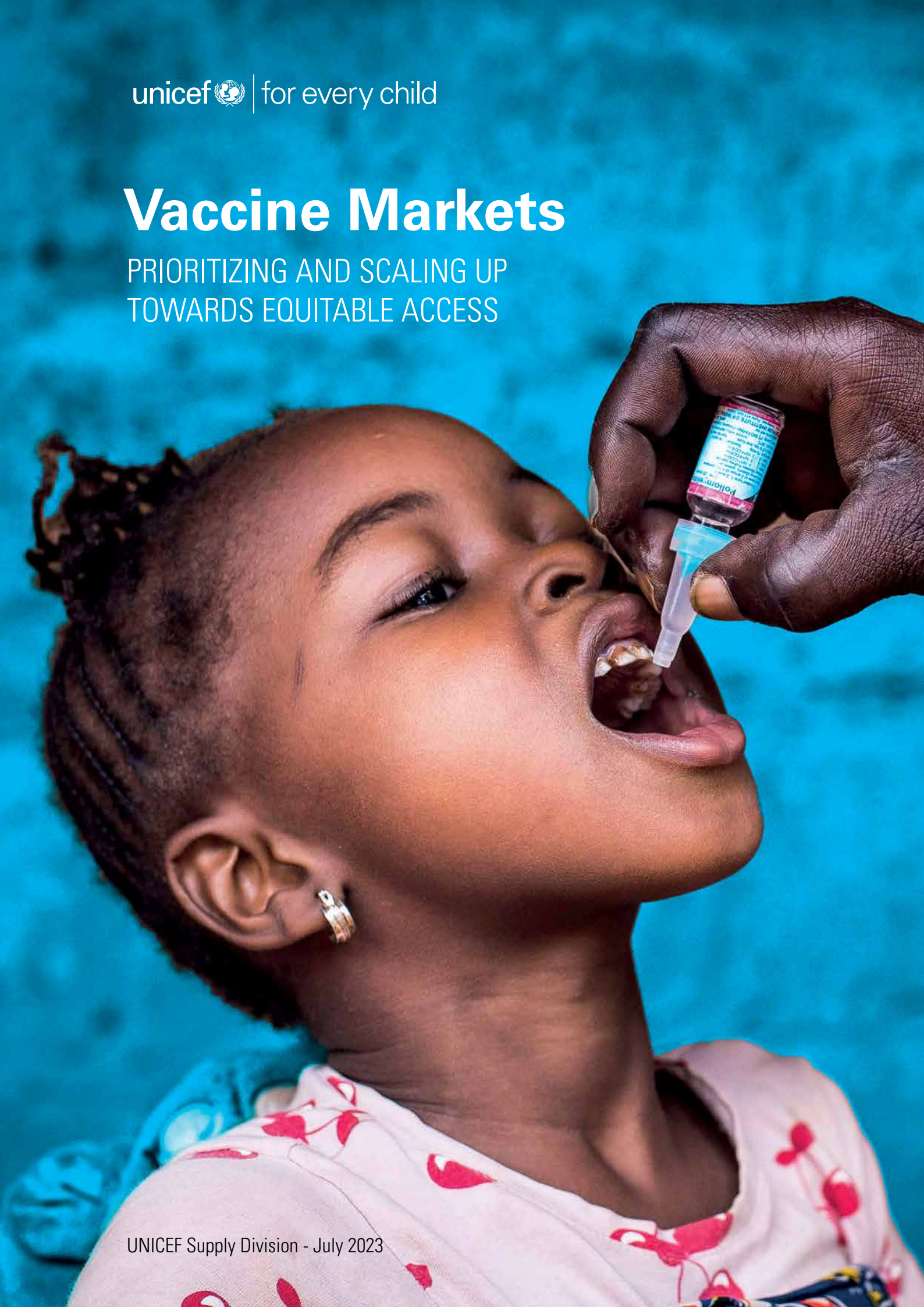
Vaccine Markets

PRIORITIZING AND SCALING UP TOWARDS EQUITABLE ACCESS



UNICEF Supply Division - July 2023

Cover photo: A child vaccinated against wild poliovirus during a national immunization day in 2014. ©UNICEF/Almeras

July 2023

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Foreword

The immense progress achieved over the past 50 years to expand access to vaccines is one of public health's greatest achievements. The vaccines available today have cut overall childhood mortality in half, allowing millions of children to experience a childhood that is free from the threat of preventable disease and lead healthy, productive lives.

On the eve of the 50th anniversary of the Expanded Programme on Immunization (EPI), we are reminded of how far we have come. Today, the cost for the standard regimen of 11 childhood vaccines is at its lowest price ever. Smallpox has been eradicated. We have vaccine stockpiles in place to quickly respond to disease outbreaks such as cholera, Ebola, meningitis, and yellow fever. The HPV vaccine is dramatically cutting rates of cervical cancer. In just one generation, the world has seen the number of children paralyzed by the polio virus decrease by 99 per cent. And we are rolling out the new malaria vaccine to protect children at risk of this deadly disease.

This progress is a testament to the scientific community, a robust vaccine industry, dedicated donors and international partners, and the commitment of national governments.

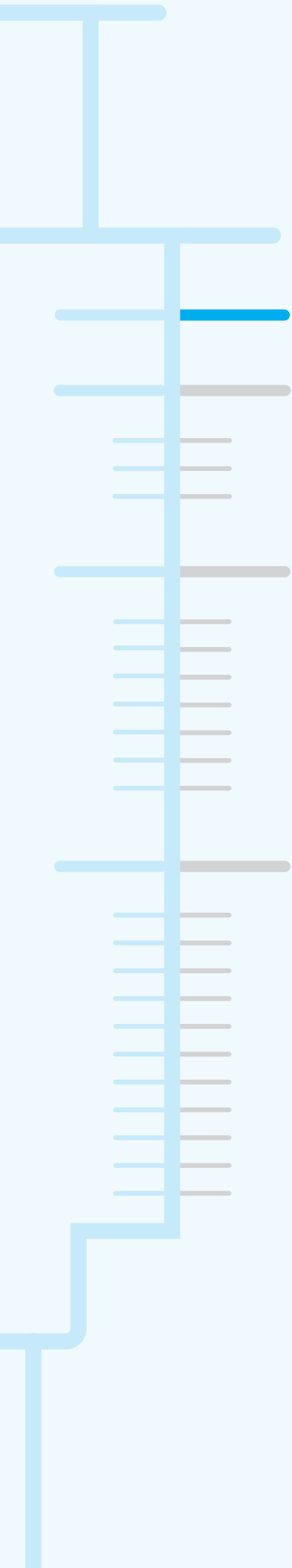
Together, these stakeholders each play a key role in driving vaccines from development to delivery - a journey that is a complex orchestra of forecasting, production, market dynamics, data systems, logistics, supply chains, and health services.

And yet, there is still more to be done. This paper sets out the challenge to accelerate action: Action to fast-track recovery of systems and address the backsliding of immunization rates in the aftermath of the COVID-19 pandemic. Action to continually improve vaccine technologies and delivery systems. Action to solve supply chain challenges and innovate for greater efficiencies for beneficiaries. And action to create sustainable vaccine markets and ensure affordability.

The impact that vaccines have had on child health globally cannot be understated. We owe it to children to continue to aspire and innovate, so that those who are born tomorrow can receive even more optimal protection from preventable disease - from childhood through adulthood. With the climate crisis heightening the risks of new diseases and outbreaks - this is all the more urgent.

Vaccines will be required in perpetuity to safeguard the health of children and their communities. UNICEF is proud to work alongside partners who have played such a critical role in this journey to date. We look forward to the next chapter as we together continue to drive innovation and access and achieve our goal of reaching every child.

Etleva Kadilli
Director, UNICEF
Supply Division



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Unless the right of every child to immunization is fully realized, equity cannot be achieved.

Marwa Abdallah poses with her three daughters after they were vaccinated against polio during the house-to-house polio campaign in Khartoum. © UNICEF/Yahya Mahjoub Osman Alfaki

This report serves as a rallying call **to secure sufficient funding for immunization**, which countries must sustain unless viruses are eradicated. Immunization is one of the most effective public health interventions ever developed, and it is the foundation of the primary health care system and an indisputable human right.[1,2] Governments and partners have achieved great progress in reducing vaccine-preventable deaths over the last decades, contributing to an ongoing global decline in under-five mortality. But the work must continue because important challenges remain.

In 2021, five million under-five children still died, most from preventable and treatable causes, of which half from infectious diseases, including pneumonia, diarrhoea, and measles,[3] and 25 million children missed out on one or all doses of diphtheria, tetanus, and pertussis (DTP).[4] This is six million more than in 2019, with the distribution of zero-dose children and coverage rates still varying widely between and within countries. Of these, 18 million children did not receive any DTP vaccine. Currently, global vaccine coverage rates have regressed as a result of the global shocks generated by the COVID-19 pandemic and ongoing multi-dimensional crises.[5] Declining vaccine coverage is resulting in increased outbreaks of diseases, such as diphtheria, polio and measles, amongst many others. Between 2019 and 2021, 67 million children missed out entirely or partially on routine immunization, of which 48 million children missed out entirely.[6]

1 World Health Organization, *Immunization Agenda 2030: A Global Strategy to Leave No One Behind*, WHO, Geneva, April 2020.
2 World Health Organization, *Child Mortality (Under-five Years)*, WHO, Geneva, January 2022
3 UNICEF, *Under-five Mortality*, UNICEF, New York, 2023.
4 World Health Organization, *COVID-19 Pandemic Fuels Largest Continued Backslide in Vaccinations in Three Decades*, WHO, Geneva, July 2022.
5 Ibid.
6 UNICEF, *The State of the World's Children 2023: For every child, vaccination*, UNICEF Innocenti–Global Office of Research and Foresight, Florence, April 2023, p. v.

Children born just before the pandemic are moving past the age when they would normally be vaccinated.

This report shines a spotlight on immunization supplies and partnerships and UNICEF's engagement in critical immunization initiatives as well as some of the efforts that have been made over the last 50 years. It details some of the key challenges and explains how UNICEF and partners will work together to achieve the overarching strategic goals to ensure a greater impact on quality of life.

Since its inception in 1946, UNICEF has been working to improve the health and well-being of children worldwide, with one of its core focus areas being immunization. UNICEF procures vaccines to reach 45 per cent of the world's children under-five. It works with partners to procure and distribute vaccines to countries that need them most. UNICEF's procurement enables it to negotiate lower prices and ensures that vaccines are available for the most vulnerable populations, including children living in remote and hard-to-reach areas. UNICEF works with global health partners to support governments to build strong immunization systems that can deliver vaccines to all children, regardless of location or socioeconomic status. This includes training healthcare workers, improving supply chains, and strengthening data systems to track vaccine coverage and target areas of low coverage. UNICEF advocates for the importance of immunization and supports governments in raising awareness among parents, caregivers, and communities about the benefits of vaccines and addressing misinformation and myths about vaccines and building trust in vaccines and immunization programmes.

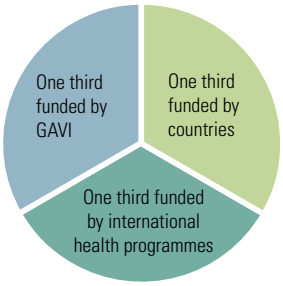
Peru, 2021. UNICEF facilitated the purchase of 1,100 solar freezers to help Peru implement the cold chain for vaccine storage and handling. @UNICEF/Vilca

Overall, UNICEF's support in global efforts on immunization has contributed to significant gains in child health around the world. UNICEF has been a critical partner in the fight against polio by securing vaccine doses to protect millions of children and contributing to the near eradication of the disease. UNICEF also played a vital role in the global effort to increase access to the pneumococcal conjugate vaccine (PCV), which has helped reduce child mortality from pneumonia, one of the leading causes of death among children under-five. The mass vaccination campaigns carried out by countries using the meningococcal conjugate A (MenA) vaccine have been highly effective and have contributed to drastically reducing the number of meningitis cases in Africa, with the rollout in routine immunization programmes enabled through funding from Gavi, the Vaccine Alliance (Gavi). Whereas the majority of meningitis epidemics were caused by meningitis A, responsible for 80 - 85 per cent of cases, since the introduction of MenA vaccine, the overall incidence of meningitis caused by serotype A was gradually eliminated in 16 countries in the meningitis belt,[7] and recent meningitis epidemics are now primarily due to serogroups C, W, and X. The UNICEF and Gavi partnership also made the pentavalent vaccine available and affordable for developing countries and resulted in a weighted average price (WAP) per dose parity for all countries.

7 Simonetta Viviani, *Efficacy and Effectiveness of the Meningococcal Conjugate Group A Vaccine MenAfriVac® in Preventing Recurrent Meningitis Epidemics in Sub-Saharan Africa*, Vaccines 10(4):617, Basel, April 2022.

2.1 Milestones in vaccine availability

Out of all the measures making up public health programmes, immunization is recognized as one of the most successful public health interventions ever developed,[8] and is the foundation of the primary health care system. UNICEF has been a leading partner in making vaccines more available and affordable to lower middle- and low-income countries (LMICs and LICs). With the collaboration of partners, UNICEF generally procures 28 different vaccines on behalf of 123 countries, which can vary from year to year, making it the largest global buyer of vaccines. Out of approximately 2.4 billion doses procured annually, approximately one third is funded by countries; one third is funded by international health programmes such as the Global Polio Eradication Initiative (GPEI); and about one third is funded on behalf of countries by Gavi, the Vaccine Alliance. UNICEF leads this work with partners on a global scale, contributing to ground-breaking and successful financing and market-shaping initiatives that helped to bring vaccination rates up over the years. UNICEF has been supplying these vaccines to reach 45 per cent of the world's children under-five years of age, ensuring that countries have access to affordable, quality-assured vaccines for every child. UNICEF works with partners to deliver vaccines from end to end, including engaging countries to generate demand, supporting decision-making processes, and strengthening supply chains, amongst other aspects. UNICEF's procurement and supply of vaccines is part of these concerted efforts to save lives and help children thrive.



8 World Health Organization, *Immunization Coverage*, WHO, Geneva, July 2022.

On 15 December 2022 in Litoral, Bolivia, healthcare worker Mercedes Parada administers a vaccine to 7-month-old Ciro, who is held by his mother, Nicoles Flores, as Ciro's 2-year-old sister, Sonia, looks on. © UNICEF/ Radoslaw Czajkowskito

2.2 Global immunization initiatives and programmes

UNICEF has had a long-standing commitment and engagement in promoting the use of and expanding access to vaccines to help prevent child mortality. Propelled and encouraged by the progress made by the **global eradication of smallpox**,[9] launched by the World Health Organization (WHO) in 1959, this initiative targeted one of the deadliest diseases to humans, and was eliminated from South America in 1971, Asia in 1975, and Africa in 1977, and finally declared globally eradicated in 1980. Smallpox eradication set the bar and the goal of eradicating other diseases and triggered many major global immunization-related initiatives.

The Expanded Programme of Immunization (EPI) was launched by the World Health Assembly in 1974, encouraged by the intensification of the smallpox eradication programme in 1967. The EPI aimed to address the poor immunization rates seen in developing countries. Immunization coverage at that time only reached five per cent of children. It targeted the need to increase immunization rates for six diseases: tuberculosis (TB), diphtheria, tetanus, pertussis, measles, and polio.[10] It included the world's first combination vaccine, which since 1948, incorporated the three antigens of DTP into one, thereby reducing the number of inoculations a child had to cope with while increasing coverage. These vaccines were later reformulated to include hepatitis B (HepB)[11] and Haemophilus influenzae type B (Hib),[12] and are soon to be further expanded to include inactivated poliovirus vaccines

9 World Health Organization, *Smallpox Eradication Programme 1966-1980*, WHO, Geneva, May 2010.
10 World Health Organization, *A Brief History of Vaccination*, WHO, Geneva, 2022.
11 World Health Organization, *Introduction of Hepatitis B Vaccine into Childhood Immunization Services*, WHO, Geneva, November 2001.
12 World Health Organization, *Introduction of Haemophilus Influenzae Type B Vaccine into Immunization Programmes*, WHO, Geneva, 2000.

In response to reports of a wild polio case in neighboring Malawi after more than three decades, UNICEF and partners of the Global Polio Eradication Initiative (GPEI) are supporting the Ministry of Health for Tanzania, in undertaking nationwide vaccination efforts to reach and vaccinate every child in the country against polio. © UNICEF

On 27 August 2022, in Shekhertek, Dhaka, single-mother of three, Fatema, visits the Surjer Hashi Clinic, to vaccinate her youngest child, 4-month-old son, Hadiyat.
© UNICEF

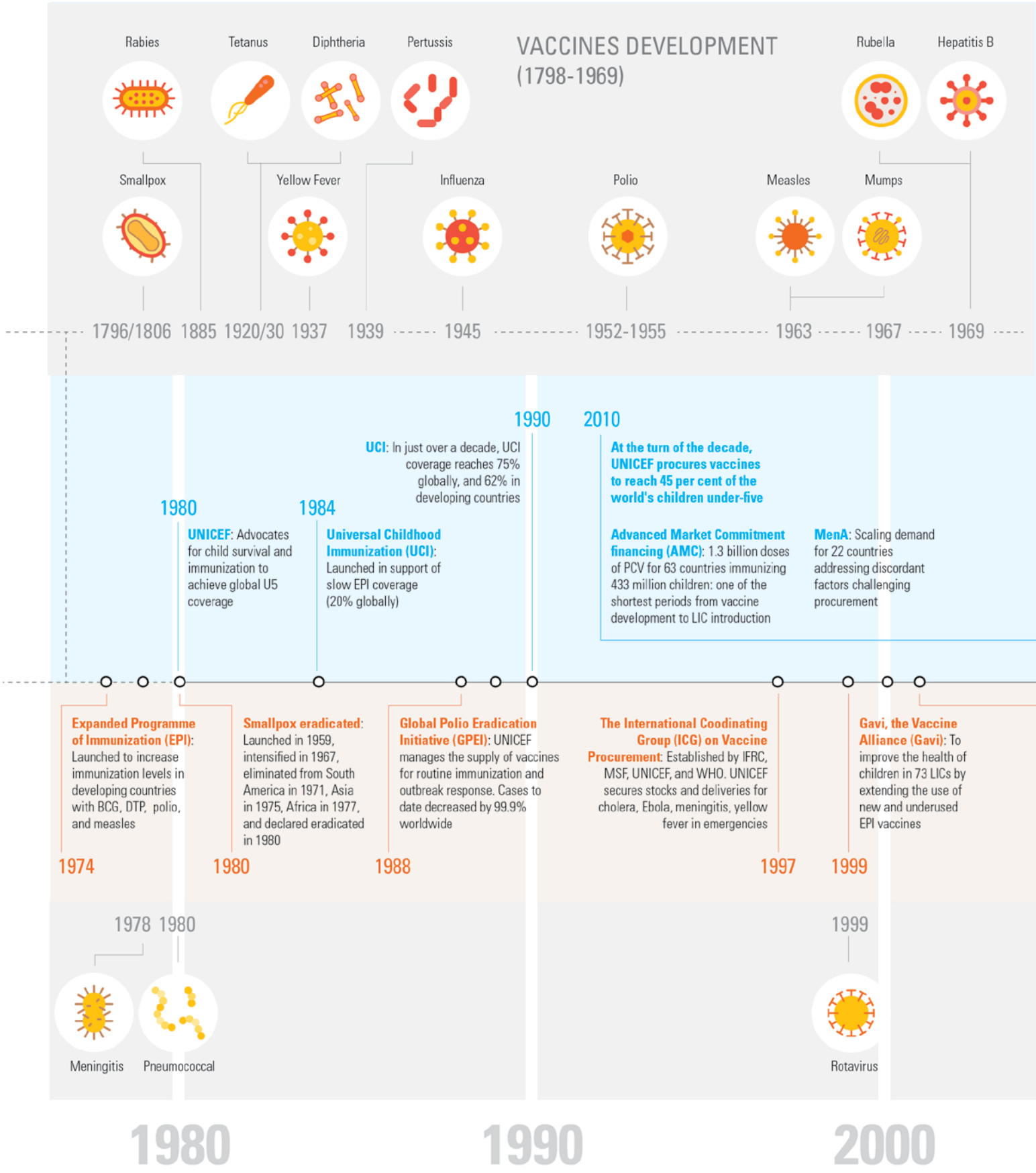
(IPV). More vaccines were added to the EPI, including pneumococcal, rotavirus, and human papillomavirus (HPV) vaccines, as well as vaccines of regional relevance in endemic countries such as Japanese encephalitis, MenA, typhoid, and yellow fever, amongst others.

UNICEF in the 1980s advocated for child survival as the progress on EPI expansion stagnated. UNICEF knew the potential impact EPI programmes could have on reducing child mortality. So it called on the need for **Universal Childhood Immunization (UCI)** in 1984, targeting a coverage rate of 80 per cent. In the 1980s, immunization only reached 20 per cent of children globally, which incorporated huge disparities between high-income countries (HICs), middle-income countries (MICs), and LICs.[13] Subsequently, by 1990, in just over a decade, UNICEF was credited with supporting countries to increase global coverage rates to 75 per cent and 62 per cent in developing countries.[14] To date, UNICEF's involvement in immunization continues, with UNICEF procuring the largest share of vaccines used in national EPI, representing 69 per cent of its procurement, with the largest share of 39 per cent being for polio campaigns and outbreak response programmes.

The Global Polio Eradication Initiative (GPEI), launched in 1988, was built on the earlier efforts of Rotary International, partnering with the US Centers for Disease Control and Prevention (CDC), UNICEF, and WHO, and includes the Bill and Melinda Gates Foundation (BMGF) and more recently, Gavi. The GPEI is driving polio eradication, initially forecasted to be achieved by 2000 and which has since been reset for 2024. To date, the GPEI has supported countries to immunize over 2.5 billion children,[15] reducing the number of cases globally by 99.9 per cent across two countries, down from 350,000 cases in 1988, and circulation has now reduced to only two countries. UNICEF secures and manages the supply of oral polio vaccines (OPV) in support of GPEI and a number of countries for routine immunization and outbreak response. While GPEI's Polio Eradication Strategy 2022 – 2026 will take countries through the final challenges to eradication, there are major issues in achieving the objective, notably the control of circulating vaccine-derived poliovirus (CVDP).[16]

13 Lindstrand, Ann, Thomas Cherian, Diana Chang-Blanc, et al., *The World of Immunization: Achievements, Challenges, and Strategic Vision for the Next Decade*, The Journal of Infectious Diseases, Vol. 224, Chicago, October 2021
14 Ibid.
15 The Global Polio Eradication Initiative, *History of Polio*, GPEI, Geneva, 2023.
16 The Global Polio Eradication Initiative, *Polio Eradication Strategy 2022–2026: Delivering on a Promise*, WHO, Geneva, June 2021.

Figure 1: TIMELINE ON THE MILESTONES OF VACCINE ENGAGEMENT



MARKET SHAPING

2001

Measles: Despite vaccine introduced in 1963 reducing outbreaks, it remains a common disease. Sharp decline in coverage in 2021 and 79% increase of cases and outbreaks

2001

Self-financing procurement: Encouraging MICs to plan and forecast demand, pool volumes to secure access and better terms through multi-year commitments

2011

Price publication: Vaccine prices made publicly available to all countries

Rotavirus: Vaccine introduction, scaling demand, reducing pricing, expanding product options, increasing coverage from 0% to 49%

2013

Market information: Market information publishing calling out issues and challenges on all vaccine products

2014

MR: New market entrants secure supply diversification, currently reliant on one dominant manufacturer

2016

Polio: Supplying 155 countries, synchronizing product changes, focusing eradication efforts on the last miles

2017

Pentavalent: five antigen combination vaccine, price reduction to less than $1 per dose, achieving affordable and sustainable pricing for children in LICs

2019

DTP: Having increased coverage from 52% in 2000 to reach 75% in 2019, across the African region helping to reduce child mortality

2021

PCV: Vaccine inroduction into 80 countries, with tail price secured for all 73 AMC countries for a 10-year period in 2022

2022

HPV: Increased access to supply for 30 LICs in support of national introductions and 15 MICs despite the supply constraints

Malaria: World's newest vaccine, access secured to supply despite constraints over the next 2-5 years

Ebola vaccine: Securing doses for outbreak response

Oral cholera vaccine: Increasing the availabilty of limited supply due to production capacity constraints

2023

CHILDHOOD COVERAGE: Despite global immunization efforts saving 4.4 million lives a year. 1 in 5 children remains unvaccinated (18.2 million zero-dose children), leaving them vulnerable to vaccine preventable diseases. 1 in 5 is not protected again measles, and 7 in 8 girls are not vaccinated against human papillomavirus. 67 million have missed out partially or entirely on routine immunization between 2019 and 2021

Hexavalent: Seeking to secure vaccine affordable and healthy market, while maintaining market for pentavalent, IPV + other DTP-containing vaccine options

COALITIONS

2001 — **The Measles & Rubella Initiative (M&RI)**: Led by the American Red Cross, BMGF, Gavi, UN Foundation, US CDC, UNICEF and WHO

2010 — **Meningitis Vaccine Project**: Launched to develop the MenA vaccine to eliminate the disease from the meningitis belt in Africa.

2016 — **The Coalition for Epidemic Preparedness Innovations (CEPI)**: To accelerate vaccine development against epidemic threats to ensure they are accessible to all

2020 — **COVAX**: The vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines

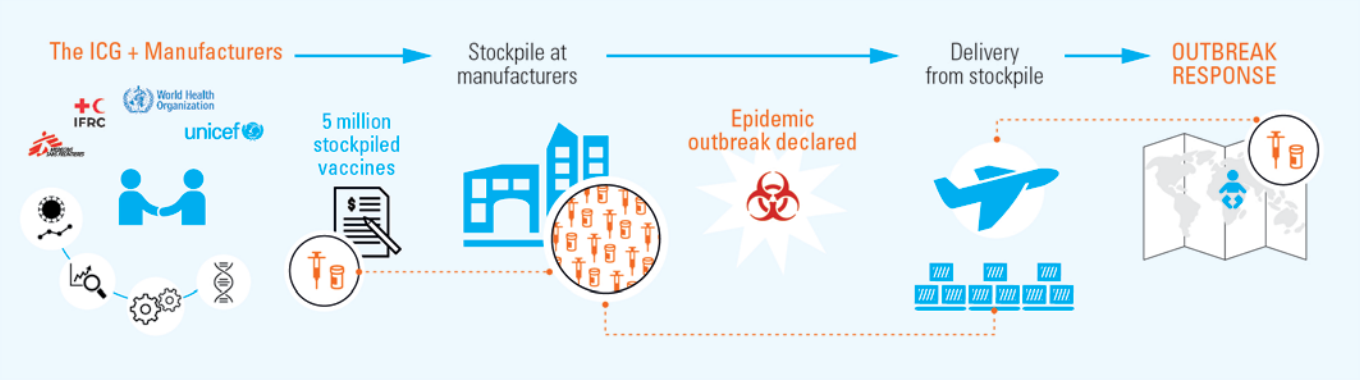
VACCINES DEVELOPMENT (1980-2021)

2010 2020

Source: UNICEF, GPEI, Gavi, WHO, MR&I, ICG, CEPI, COVAX

The International Coordinating Group (ICG) on Vaccine Provision was established in 1997 following major outbreaks of meningitis in Africa. This is a mechanism to manage and coordinate the allocation of vaccines in short supply and antibiotics to countries during major outbreaks. Timing, size, and viruses leading to epidemic disease outbreaks are by nature difficult to predict, and the strains required for an outbreak response can be difficult to forecast. This leaves people living in outbreak-prone areas at a higher risk of infectious disease outbreaks. However, some outbreaks can be contained and controlled by the rapid deployment and administration of appropriate vaccines. The ICG ensures that those vaccines that are often in limited supply and not readily available in the amounts needed to respond to emergencies in vulnerable settings are allocated where they are most needed. UNICEF contracts and manages the emergency stockpiles that have been established to bridge the gaps in vaccine supply to include cholera, Ebola, meningitis, and yellow fever vaccines. UNICEF works with programmes on the delivery of these vaccines for use in emergencies with the financial support of Gavi.

Figure 2: EMERGENCY OUTBREAK RESPONSE MECHANISM OF THE ICG



Gavi, the Vaccine Alliance. While the achievements of EPI, the eradication of smallpox, and other success stories in immunization inspired further goals targeting the elimination and eradication of vaccine-preventable diseases, especially in LICs and MICs, global immunization coverage had plateaued by the end of the 1990s. At the close of the millennium, 30 million children living in poor countries were still not fully immunized.[17] Coverage was stagnating, and in some countries, even declining. In addition, children in LICs and MICs were not given access to new vaccines that were being developed beyond those under EPI. The new vaccines developed in the 1990s, such as HepB and Hib, were only made available as industry gradually increased capacity and shifted product presentations. This typically led to a 10- to 15-year delay before LICs could access these vaccines. There were many reasons for this. One of the most important factors was that the pricing of vaccines was too high, and many vaccine product presentations were not suited for use in LICs. There were also issues related to the lack of information on both the price and the different vaccine product characteristics, which many countries found were limiting their ability to make decisions and implement affordable and effective immunization programmes.[18]

In 2000, a grand public-private coalition made up of BMGF, UN agencies and institutions (WHO, UNICEF, the World Bank), technical research institutes, donor countries, and implementing countries, the vaccine industry, and civil society organizations (CSOs), created the Global Alliance for Vaccines and Immunization (GAVI), later called Gavi, the Vaccine Alliance. Its objective was to improve the health of children in the poorest 74 countries with a gross national income (GNI) below $1,000 by accelerating access to new and underused vaccines. This initiative renewed the global interest in immunization and the control of vaccine-preventable infectious diseases. It successfully raised funding for the introduction of HepB and Hib vaccines in these countries, and together with a new and progressive co-financing policy, it set the stage for the successful introduction of pneumococcal, rotavirus, and HPV vaccines almost simultaneously with wealthier countries, mobilizing resources at scale, supporting UNICEF's efforts of shaping markets for affordability, allowing the Gavi partnership and UNICEF to procure and deliver vaccines at a record pace.

17 Gavi, the Vaccine Alliance, *Global Alliance for Vaccines and Immunisation (Gavi)*, Gavi, Geneva, 2022.
18 Médecins Sans Frontières, *The Right Shot: Extending The Reach of Affordable and Adaptable Vaccines - 1st Edition*, MSF, France, 2012, p. 2.

The Meningitis Vaccine Project was launched in 2010,[19] through an international partnership funded by BMGF, in collaboration with Gavi, PATH, UNICEF, WHO, and partners. It focused on developing, testing, licensure, and widespread introduction of a conjugate vaccine targeting group A meningococcal meningitis. UNICEF supported the mass vaccination campaigns conducted by countries in the African meningitis belt, helping to scale the demand for this vaccine on behalf of 22 countries in that region. This programme has been highly effective and has contributed to drastically reducing the number of meningitis cases in Africa. Sixteen countries in the meningitis belt have eliminated meningococcal A by progressively rolling out the vaccine through various programme activities. Post introduction, meningitis surveillance revealed that serogroup A meningococcal disease had disappeared from all age groups, suggesting that robust herd immunity had been achieved.[20]

COVAX, is the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator, a ground-breaking global collaboration to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines. COVAX is co-led by the Coalition for Epidemic Preparedness Innovations (CEPI), Gavi, and WHO, with UNICEF as a key coordinator, procurement, and delivery partner.[21] It is the most recent vaccine initiative that was able to purchase vaccines at historical scale and speed as a result of extraordinary and unique global collaboration. UNICEF with its partners CEPI, Gavi, and WHO, were part of the largest vaccine supply operation in history.[22] In January 2020, the genetic sequencing of the virus was published,

19 UNICEF, *Meningococcal Vaccine: Supply and Demand Update,* UNICEF, Copenhagen, August 2019.
20 Viviani Simonetta, *Efficacy and Effectiveness of the Meningococcal Conjugate Group A Vaccine MenAfriVac® in Preventing Recurrent Meningitis Epidemics in Sub-Saharan Africa.*
21 UNICEF, *COVAX Objectives 2022*, UNICEF, Copenhagen, April 2022.
22 UNICEF, *The State of the World's Children 2023: For every child, vaccination*, p. i.

In the Philippines, health workers Ash Abubacar and Injilah Moca, go house-to-house in the communities covered by their rural health unit to offer vaccines to children unable to visit the health centre. © UNICEF/ Martin San Diego

and by January 2021, 100 million doses had been administered globally.[23] As the lead procurement agency for COVAX, in collaboration with the Pan American Health Organization (PAHO), UNICEF has been managing the delivery of close to 2 billion COVID-19 vaccine doses to 146 countries from January 2021.

Spanning 40 years, all these programmes combined have had an incredible impact on children, and their communities, reducing the number of children dying from vaccine-preventable diseases by 70 per cent, and protecting millions more as they grow. Failure to protect children against disease has serious consequences. Put bluntly, children die, and many more suffer lifelong disabilities. In 2022, with the concerted support of global health partnerships, UNICEF procured 2.4 billion doses of paediatric vaccines for 108 countries to reach 45 per cent of the world's children under-five years old. Forty-eight per cent of these vaccines went to routine immunization programmes. The remainder supported supplementary immunization activities, outbreak response, and humanitarian situations.

23 Center for Health Security, *COVID-19 Vaccine Development Timeline*, John Hopkins Bloomberg School of Public Health, Baltimore, 2021.

A UNICEF shipment of 63 cubic metres of vital health supplies arrives in Kinshasa which was the epicentre of the COVID-19 epidemic in the Democratic Republic of the Congo (DRC). The shipment includes oxygen concentrators, basic surgical equipment, stethoscopes, antibiotics, nutrition items, kits for midwives and items for maternal and neonatal health. © UNICEF/Desjardins

2.3 UNICEF vaccine procurement

Over the past 10 years, UNICEF and partners have delivered a total of 26.4 billion doses of vaccines, with an average of 2.4 billion doses a year. In addition, UNICEF has also facilitated the delivery of 919 million COVID-19 vaccine donations globally. By far, the largest share of these vaccines procured through UNICEF was for polio, which accounts for approximately just under 50 per cent of the total annual volume reaching on average 1.4 billion doses a year in support of polio eradication. The volume of doses UNICEF has procured is gradually declining, reflecting the decline in polio activities due to the progress towards the eradication of wild poliovirus. In 2020, there was a dip showing the impact the COVID-19 pandemic had on immunization programmes as countries went into lockdown, which had a major toll on public health programmes, including immunization activities. From 2021, UNICEF increased its procurement volume, reflecting the delivery of COVID-19 vaccines in response to the pandemic in favour of LICs and MICs.

See Figures 3 and 4 on next page

Figures 3 and 4: VACCINE PROCUREMENT THROUGH UNICEF

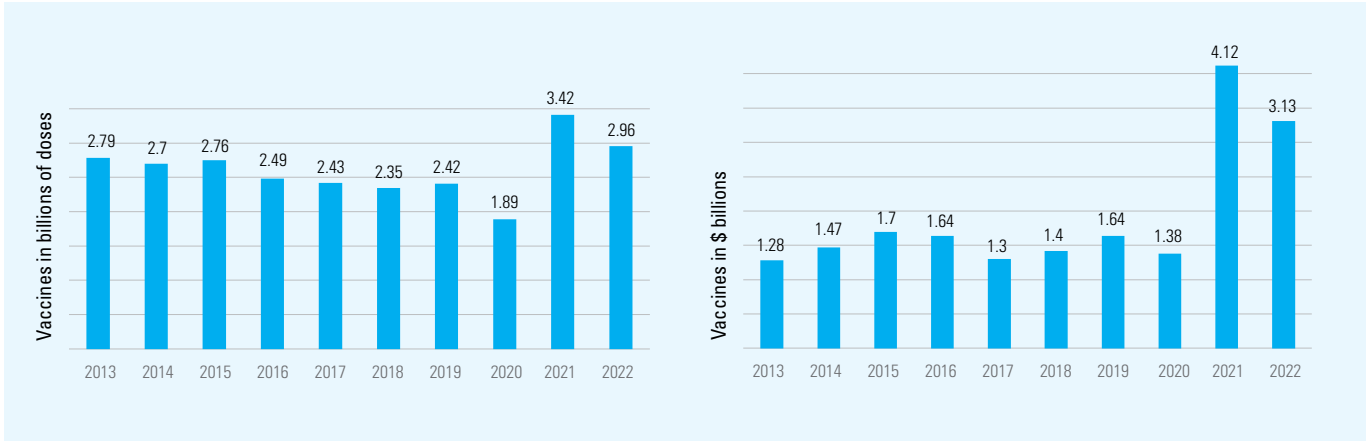


Figure 5: DISTRIBUTION OF UNICEF-PROCURED VACCINES IN 2022 (by number of doses)

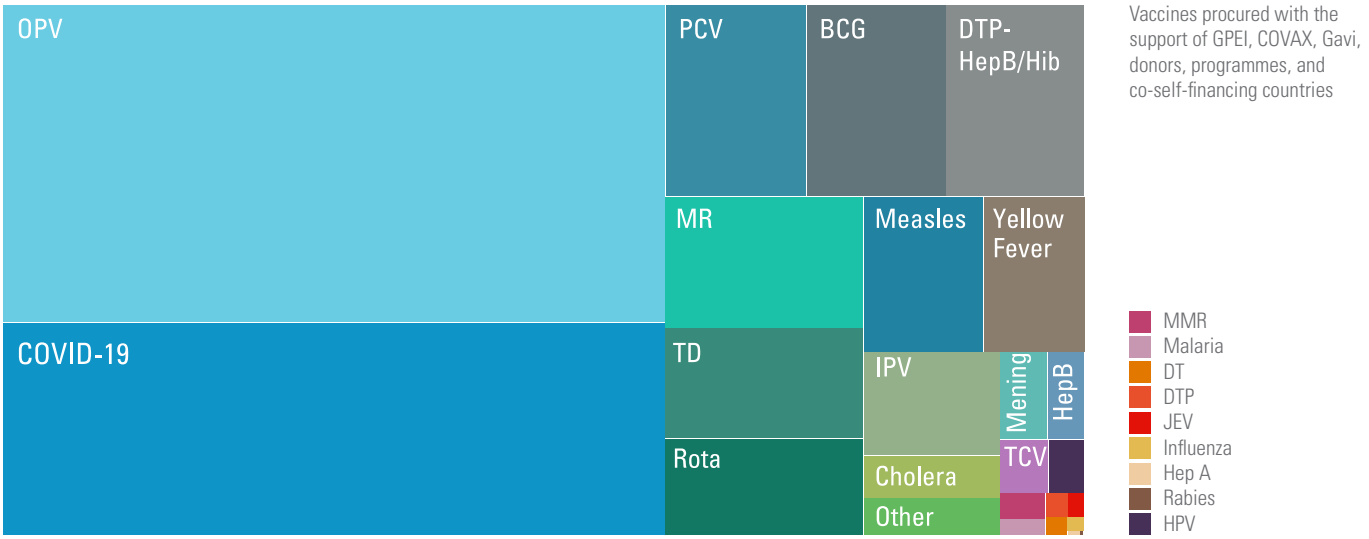
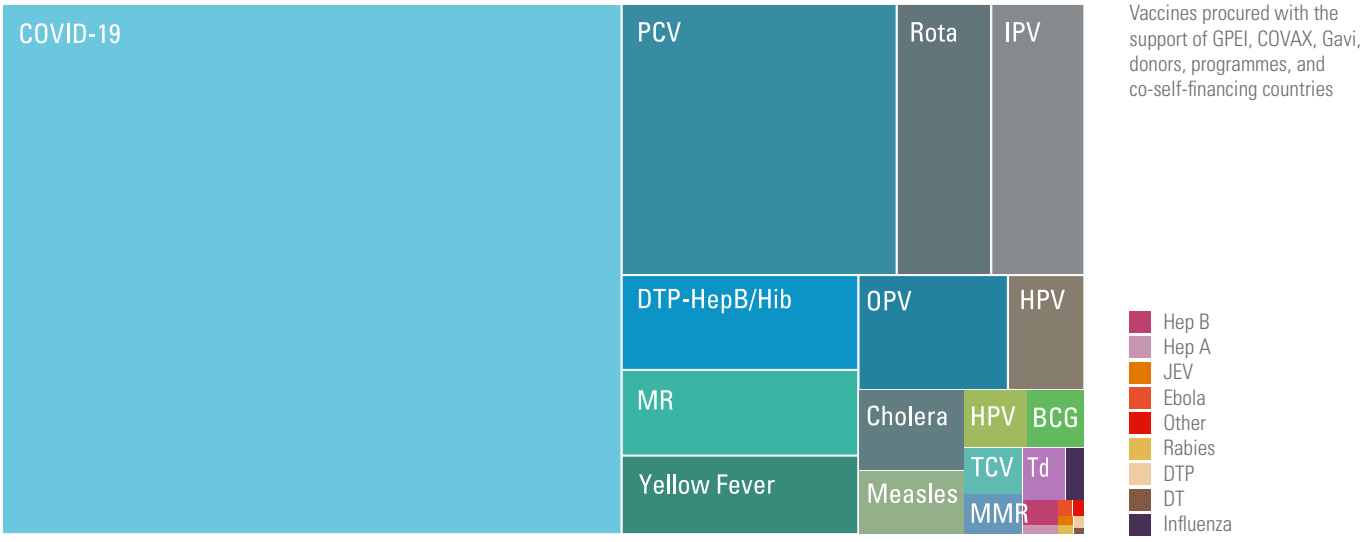


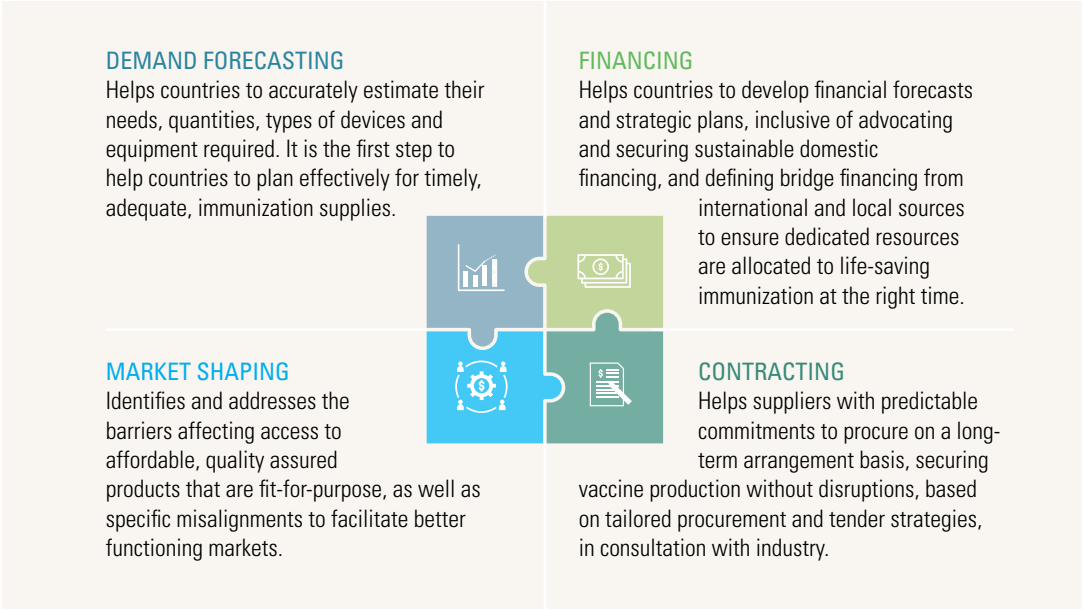
Figure 6: DISTRIBUTION OF UNICEF-PROCURED VACCINES IN 2022 (by $ value)



UNICEF's procurement over the same time period reached $19.2 billion. Prior to COVID-19, UNICEF's vaccine procurement averaged $1.5 billion a year, fluctuating between $1.3 billion and $1.9 billion. It reached a record of $4.1 billion in 2021 on account of its $2.6 billion procurement of COVID-19 vaccines on behalf of LICs and MICs, which even though high, represents only a small fraction of the total global spend on COVID-19 vaccines.

UNICEF's pooled procurement of vaccines and its engagement with partners in vaccine markets seeks to ensure vaccine security and the sustained uninterrupted supply of the quality, affordable vaccines children need. By bringing the cost of vaccines to more affordable levels, price savings have allowed countries to access more for less and increase immunization coverage. UNICEF and its partners use strategic procurement, long-term forecasting, special contracting terms, multi-year arrangements, as well as price and information transparency to provide longer-term visibility on levels of demand for essential products, including vaccines. These activities have strengthened partner collaboration through joint forecasting and pooled procurement, which in turn, have enabled suppliers to plan and scale up production, and increased the availability of affordable supplies for every child. These collaborative approaches have been able to diversify suppliers as well as introduce new and more effective products. With the invaluable collaboration of partners, multi-year contracts and innovative financing mechanisms have also contributed to achieving price reductions. Over the past ten years, UNICEF has realized savings reaching $2.7 billion in vaccine procurement. This represents an average of $272 million a year. Price reductions in pentavalent and rotavirus vaccines (RV) alone account for 60 per cent of these price savings, followed by HPV, IPV, and PCV vaccines accounting for another 38 per cent.

Figure 7: UNICEF INFLUENCING MARKETS



Besides access and pricing, one of the biggest issues that limited the ability of countries to increase vaccine procurement and coverage was the lack of information on different product characteristics.[24] UNICEF has worked with a diverse set of suppliers in different geographies under the oversight of different regulatory authorities, looking at vaccine availability, access, affordability, market competition, and product quality, as well as their acceptability and adaptability to the contexts where they are used. This includes how they are shipped, transported, and delivered, as well as how they are administered. UNICEF employs a number of strategic tools and approaches in vaccine procurement, including through innovative procurement strategies, tender approaches, vaccine industry consultations, the use of dashboards and market communication, nurturing and developing manufacturer relationships, including early-stage developers, as well as information transparency and advocacy. These enable informed, active decision-making and foster healthy competition.

24 MSF, *The Right Shot: Extending the Reach of Affordable and Adapted Vaccines*, p. 2.

3. Current issues in vaccine markets

3.1 The impact of the COVID-19 pandemic on immunization coverage

By 2019, the global coverage of immunization reached 86 per cent of all children under-five years of age, as measured by DTP1 coverage, albeit with significant disparities in antigens and countries, and which equated to approximately 577.5 million children out of an estimated total under-five population of 671.5 million.[25] However, between 2019 and 2021, 67 million children missed out entirely or partially on routine immunization, of which 48 million children missed out entirely.[26] Children born just before the pandemic are moving past the age when they would normally be vaccinated according to routine immunization schedules.

Figure 8: IMMUNIZATION COVERAGE 2021

Vaccine	
DTP 	DTP: Global coverage of DTP3 fell from 86 per cent in 2019 to 81 per cent in 2021, its lowest level since 2008. The latest WHO and UNICEF estimates of national immunization coverage also show that 112 countries experienced stagnant or declining DTP3 coverage since 2019 with 62 of those countries declining by at least five percentage points. As a result, 25 million children were un- or under-vaccinated in 2021 where more than 60 per cent live in just 10 countries (Angola, Brazil, DRC, Ethiopia, India, Indonesia, Myanmar, Nigeria, Pakistan, and the Philippines) and 18 million did not receive any, pointing to a lack of access to immunization and other health services, and an additional 6.8 million are partially vaccinated.
HepB 	HepB for infants had been introduced nationwide in 190 Member States by the end of 2021. Global coverage with 3 doses of hepatitis B vaccine is estimated at 80 per cent. In addition, 111 Member States introduced nationwide 1 dose of hepatitis B vaccine to newborns within the first 24 hours of life. Global coverage is 42 per cent and is as high as 78 per cent in the Western Pacific region, while it is only estimated to be at 17 per cent in Africa.
Hib 	Hib has been introduced in 192 countries by the end of 2021. the Hib vaccine had with a global coverage rate with 3 doses of Hib vaccine reaching an estimated 71 per cent, although there is a wide variation between regions. Whereas the Eastern Mediterranean region and South-East Asia region reached an estimated 82 per cent coverage, the Western Pacific region only reached 29 per cent.
HPV 	HPV has been introduced into 116 countries by the end of 2021. Since many large countries have not yet introduced the vaccine and vaccine coverage decreased in 2021 in many countries, global coverage with the first dose of HPV among girls is now estimated at 15 per cent. This is a proportionally large reduction from 20 per cent in 2019.
Measles 	Measles: By the end of 2021, 81 per cent of children had received 1 dose of measles-containing vaccine by their second birthday. 183 countries had included a second dose as part of routine immunization, and 71 per cent of children received 2 doses of measles vaccine.
Mumps 	Mumps had been introduced nationwide in 123 countries by the end of 2021.
PCV 	PCV had been introduced in 154 Member States by the end of 2021, including a second dose in parts of some countries, and global third dose coverage was estimated at 51 per cent. There is great variation between regions, with Europe estimated to have 82 per cent coverage, while it is only 19 per cent in the Western Pacific.
Polio 	Polio's third dose was given in 2021 to 80 per cent of infants around the world. In 2021, the coverage of infants receiving their first dose of IPV in countries that are still using OPV is estimated at 79 per cent. Targeted for global eradication, wild polioviruses have been stopped in all countries except for Afghanistan and Pakistan. Until poliovirus transmission is interrupted in these countries, all countries remain at risk of importation of polio, especially countries with weak public health and immunization services and travel or trade links to endemic countries.
Rotavirus 	Rotaviruses was introduced in 118 countries by the end of 2021, including 2 doses in some parts of the country. Global coverage is estimated at 49 per cent.

25 United Nations, *World Population Prospects 2022*, Department of Economic and Social Affairs, Population Division, UN, New York, 2022.
26 UNICEF, *The State of the World's Children 2023: For every child, vaccination*, p. v.

Rubella		Rubella was introduced nationwide in 173 countries by the end of 2021, and global coverage is estimated at 66 per cent.
Yellow fever		Yellow fever vaccine, as of 2021, had been introduced in routine infant immunization programmes in 36 of the 40 countries and territories at risk for yellow fever in Africa and the Americas. In these 40 countries and territories, coverage is estimated at 47 per cent.

Source: World Health Organization, Immunization Coverage, WHO, Geneva, July 2022.[27]

The COVID-19 pandemic affected the ability of countries to access life-saving supplies such as vaccines. It applied pressure on manufacturers, supply, as well as logistics, putting at risk the continuation of immunization programmes in countries due to lockdowns and other measures enforced to contain the spread of the virus. Manufacturers ended up carrying significant inventories because many countries dramatically stopped their uptake of vaccines in March 2020. However, at the same time, manufacturers were encouraged to continue vaccine production, as though the temporary suspension of immunization programmes would be short-lived and soon resolved. During the acute stages of the pandemic, when many manufacturers also faced challenges in accessing raw materials to produce vaccines for routine immunization, some switched their production to COVID-19 vaccines. Capacity was constrained at packaging sites, and national regulatory authorities accumulated backlogs to release products, all of which affected the shipment of vaccines.

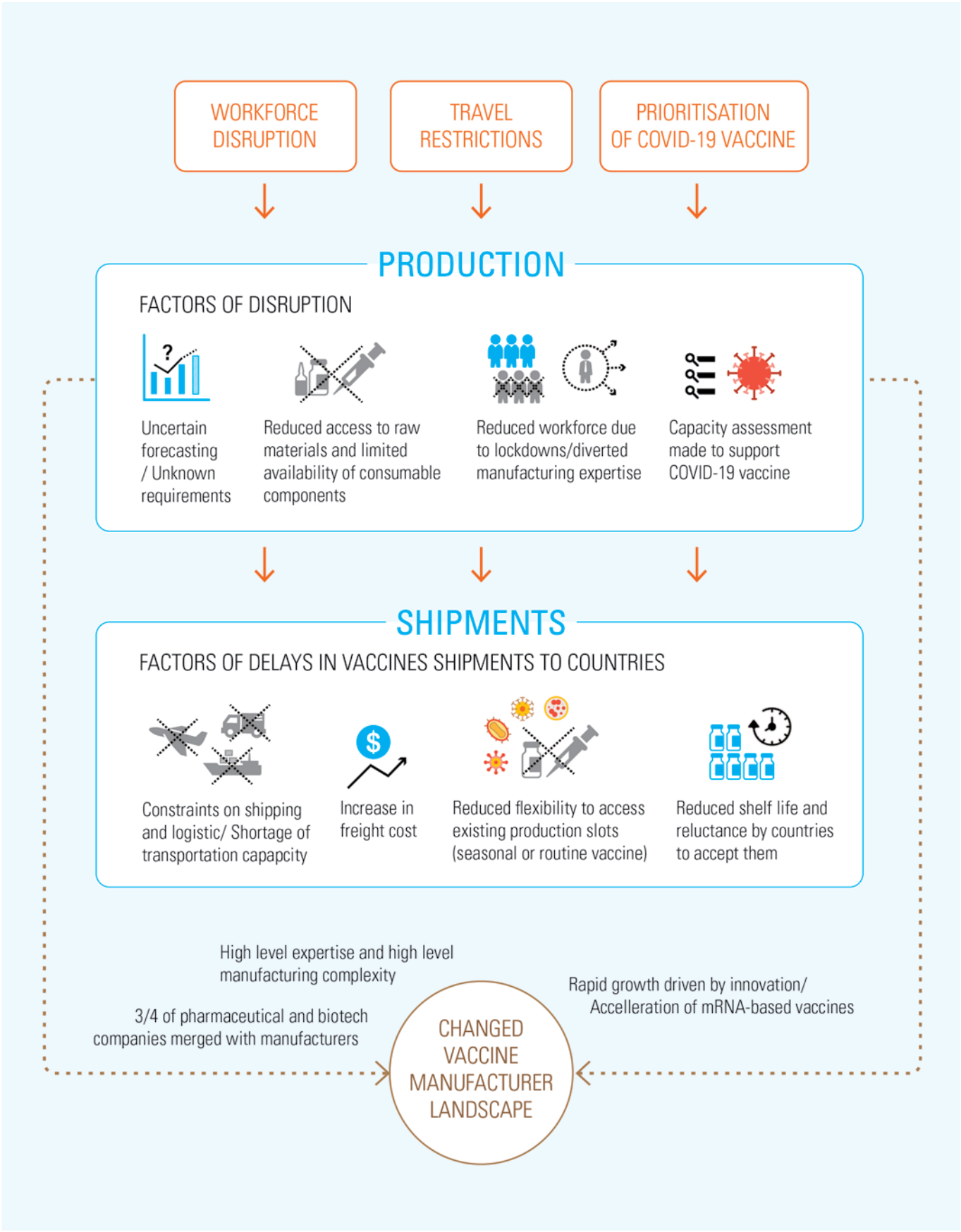
During 2020, there was the collapse in the airline industry, which impacted the shipments of vaccines significantly. As programme activities on the ground stopped abruptly in many countries, UNICEF used special monitoring and priority-setting procedures to facilitate ongoing shipments to countries at risk of stock outs while ample supplies were held at supplier warehouses. COVID-19 lockdowns interrupted the provision of health services, and as a result, global immunization rates dropped to 81 per cent, representing a decline affecting approximately 33.5 million children. An estimated 25 million children under the age of one year did not receive basic vaccines, which is the highest number since 2009.[28]

Even though global vaccination continued to decline in 2021 with 25 million children missing out on life-saving vaccines, which was two million more than in 2020, and 6 million more than in 2019, all manufacturers continued producing childhood routine immunization vaccines. Key challenges reported by some suppliers due to the delays in vaccine shipments included:

- Ticking shelf-life of vaccine products that were produced according to forecasts but not shipped, as well as the reluctance by countries to accept products with a reduced shelf-life.
- Delay for the planned production of seasonal vaccines, such as influenza, as capacity was reallocated to support COVID-19 vaccine manufacturing.
- Difficulty obtaining raw materials due to increased lead times, and production were prioritized for domestic use and the COVID-19 vaccine.
- Difficulty in accessing consumable components such as filters, tubing, vials, syringes, and ampoules, sometimes due to export barriers.
- Cash flow challenges as projected revenues were not materializing.
- The overall fill and finish capacity of some vaccine manufacturers, both internal and outsourced, faced bottlenecks due to the production of COVID-19 vaccines being prioritized.
- Unprecedented reliance on companies subcontracted to manufacture products on manufacturers' behalf, known as contract manufacturing organizations (CMOs), for parts of the COVID-19 vaccine production process and integration of these new approaches on some accounts.
- Delayed batch releases of routine immunization vaccines by manufacturers and national regulatory authorities (NRAs) as the release of COVID-19 vaccines were prioritized.
- Shortage of transportation capacity combined with a significant increase in freight costs, which had more than tripled.[29]

27 WHO, *Immunization Coverage*.
28 Ibid.
29 UNICEF, *COVID-19 Impact Assessment on Global Logistics and Supplies*, UNICEF, Copenhagen, September 2021.

Figure 9: KEY CHALLENGES FOR ROUTINE IMMUNIZATION



At the start of 2023, UNICEF has been noticing improvements in several critical areas of transport and shipping, including booking lead times. However, challenges remain for many countries. The International Monetary Fund (IMF) reported global inflation to have risen from 4.7 per cent in 2021 to 8.8 per cent in 2022. Even though this has since declined to 6.5 per cent in 2023, the IMF anticipates inflation will reach 4.1 per cent by 2024; it will still represent a significant burden on a country's fiscal space, with consequences on government budgets to ensure social services.[30] The IMF projects global growth to fall to 2.9 per cent in 2023. However, rising interest rates and the war in Ukraine continue to weigh heavily on global economic activity. According to the Organization for Economic Co-operation and Development (OECD), despite the early signs of recovery, the war in Ukraine continues to overshadow the world economy and will likely result in only moderate recovery over the next two years.[31] The global outlook remains fragile, and the risks to a downside will predominate with trade tensions remaining high and which could worsen. Concerns of financial vulnerability have also increased, including among financial institutions and LICs. Multi-dimensional crises, including conflict, global inflation, and falling global growth, will make funding public health services for children a challenge going forward.

3.2 UNICEF risk mitigation strategies in vaccine procurement

Through four decades in vaccine procurement, including during the COVID-19 pandemic, UNICEF has identified a number of issues and documented lessons learned that have informed mitigation strategies.

- Manufacturers often overestimate their capacity to scale up vaccine production and underestimate the time taken to get their product to market and ensure product delivery. As such, UNICEF and suppliers set clear milestones and closely monitor product development and regulatory timelines, as well as supply plans, and agreements to ensure there is a constant visibility on changes and focused discussions on margins. This allows UNICEF to take early actions to mitigate any risk to immunization programmes. This addresses what are often wide margins of best-case assumptions.
- Close coordination and visibility also help UNICEF identify problems early on and mitigate the risk of manufacturing lines becoming subject to technical errors and delays. This includes prequalification and regulatory approvals, which would directly impact the timing of supply to support programmes.
- Country demand forecast accuracy has had a significant impact on the availability and access to supply. Suppliers seek to have, ideally, long-term visibility on forecast demand to ensure access to raw materials and optimize their use of production resources. However, a country's conversion of demand forecasts into actual demand is linked to the availability of funding.
- UNICEF has a number of tools to assist with bridge financing, such as the Vaccine Independence Initiative (VII),[32] which helps countries to procure vaccines. BMGF, Gavi, and other donors are major financial resources and have been critical to assisting LICs and MICs to address critical supply gaps in immunization programmes.
- While timely forecasts can help secure supply, cases of sudden increases in demand may lead to increase in prices, as expanded supply may require investments that need to be recovered. Price reductions often rather come from being linked to reaching certain volumes.
- National information management systems are critical for stock and inventory management and reporting. To avoid the expiry of stocks, as well as stock outs, there is a need to understand demand requirements beyond central stores. UNICEF provides EPI managers with a visibility tool for vaccines (ViVa),[33] which is an online stock projection dashboard that visualizes the pipeline of vaccine orders and forecasts, as well as the stock levels under certain demand scenarios. It is a tool for EPI managers who do not have access to alternative digital platforms. ViVa creates alerts and recommendations, enabling governments to identify the risks of a stock out or overstocking and take preventive action. Countries can use ViVa to increase their use of data in the management of vaccine supply chains.
- Programmatic suitability, vaccine interchangeability, and pricing affordability are key considerations for MICs to decide on introducing new vaccines, and for which UNICEF advises countries by providing

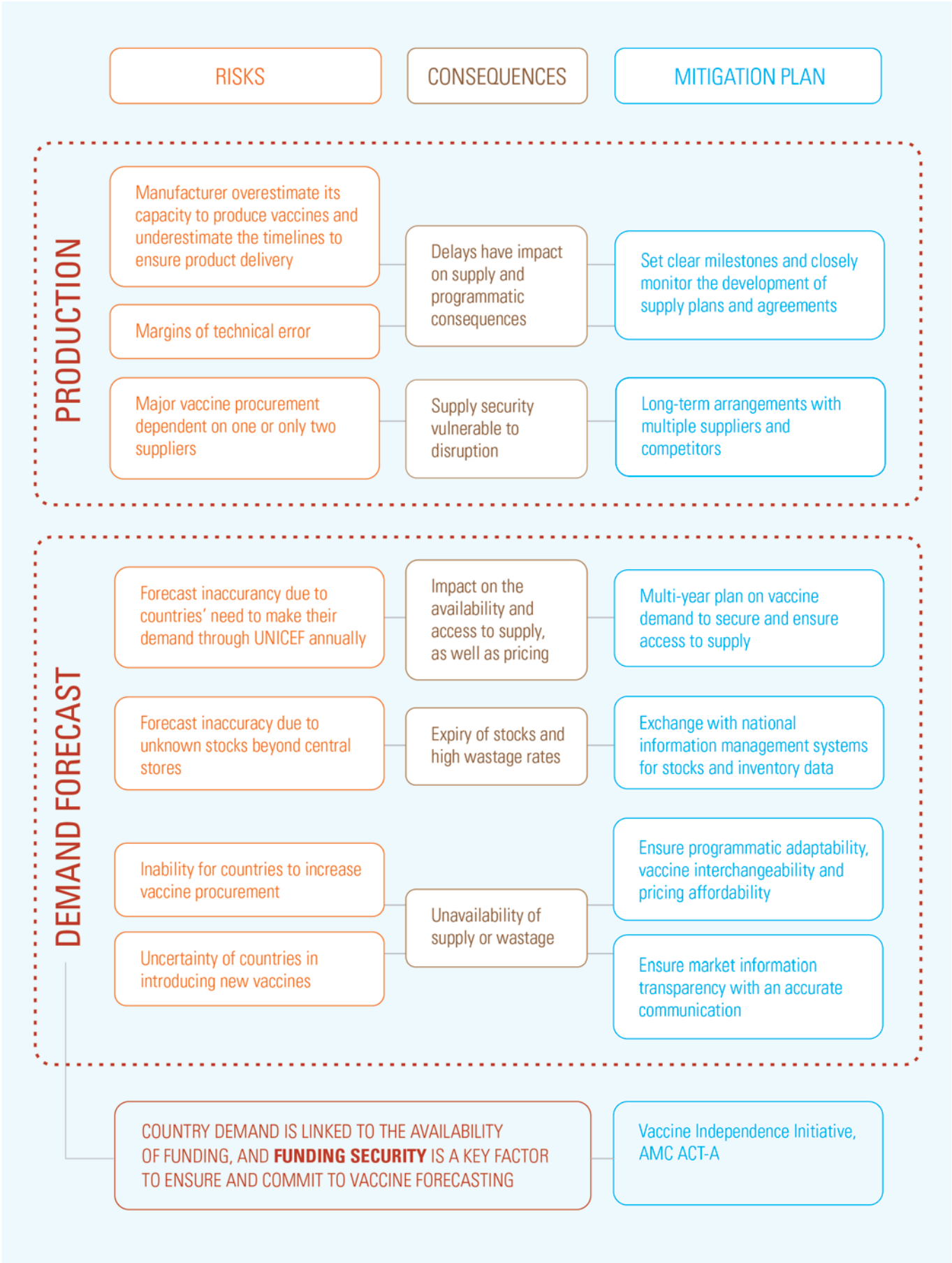
30 International Monetary Fund, *World Economic Outlook*, IMF, Washington, March 2023.
31 Organization for Economic Co-operation and Development, *A Fragile Recovery*, OECD, Paris, March 2023.
32 UNICEF, *Supply Financing*, UNICEF, Copenhagen, June 2020.
33 UNICEF, *Visibility for Vaccines*, UNICEF, Copenhagen, 2022.

procurement considerations based on market information, programmatic understanding and considerations.

- In order to assist countries in accessing supplies and improve commercial terms, UNICEF advises countries to make multi-year commitments, as the lack of longer-term solid demand planning from MICs makes it difficult for UNICEF to ensure effective procurement interventions, including the ability to optimize terms, conditions and pricing.
- The risk to supply security can be high if not appropriately mitigated. Out of the 57 long-term arrangements UNICEF has with suppliers for the procurement of vaccines, 22 of them are with South Asia-based manufacturers. Seven of UNICEF's vaccines are sourced from one supplier, and seven are dependent on two suppliers, with the remainder having three or more suppliers. Many markets remain heavily reliant on one manufacturer due to significant differences in production capacity between manufacturers. Around 48 per cent of WHO-prequalified products supplied through UNICEF are produced in only one country and cleared by the same NRA, which makes these vaccines highly dependent on one country's regulatory capacity and susceptible to supply constraints should disruptions occur. As such, UNICEF's market shaping efforts with partners seek to diversify its supplier base, including awarding multiple suppliers across a diverse geography, encourage new market entrants where there is insufficient capacity or an imbalanced competitive market, and include regionalizing vaccine suppliers. Market information communication is one of the key tools to ensure market transparency and address information asymmetry in vaccine market understanding.

Health worker Sumiati prepares to administer the polio vaccine to students at Langsa Primary School in Indonesia. WHO declared Indonesia and the rest of the region of Southeast Asia polio free in 2014. However, low immunization coverage in the country – which has been exacerbated by the COVID-19 pandemic, socio-cultural sentiments around vaccination and unhealthy environmental conditions – has slowed efforts toward polio eradication. © UNICEF/ Ulit Ifansasti

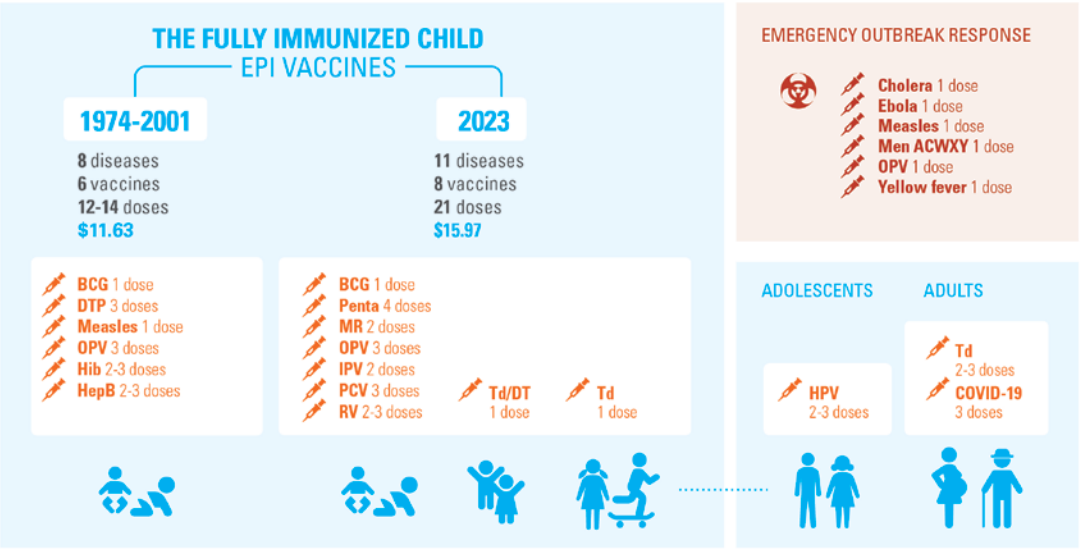
Figure 10: UNICEF RISK MITIGATION STRATEGIES



3.3 The fully immunized child: then and now

UNICEF's procurement of vaccines aims to achieve vaccine security through the uninterrupted sustainable supply of affordable vaccines of assured quality and relies on WHO's prequalification system and its assessment of quality, safety, and efficacy. UNICEF also seeks to diversify its sources of safe and cost-effective supply of vaccines globally. Over the years, this is increasing. In 2001, the total cost of purchasing a full course of six EPI vaccines through UNICEF averaged $11.63 per child, made up of Bacillus Calmette-Guerin (BCG) for TB, DTP-Hib-HepB, measles, and polio.[34, 35] WHO's recommended summary of vaccines for all routine immunization needs for children has since increased to 11 antigens. The changes include replacing the DTP vaccine with pentavalent (DTP-HepB-Hib); monovalent measles with measles and rubella (MR); and the addition of IPV, PCV, and RV, as well as the use of tetanus and diphtheria (Td) booster vaccines. This has increased the total number of doses to 21 if administered through the optimal choice of the least number of vaccines.[36] In 2013, the cost for the new regimen of vaccines to fully immunize a child through UNICEF reached $24.46. The cost difference was on account of the relatively high prices for newer vaccines, including pentavalent, PCV and IPV. **However, UNICEF with its partners, through market shaping efforts, decreased this cost to $19.13 in 2016 and to $16.24 in 2017. As of 2023, this cost has been reduced to $15.97 and represents a decrease of 35 per cent over 10 years**.[37] The final costs for vaccines depend on the country's choice of schedule, compliance with WHO recommendations, vaccine product and presentation, country income level, procurement terms and conditions, as well as other decision-making factors. This data excludes provisions made for wastage, landed costs, and all programmatic administration and considerations.

Figure 11: TREND IN FULLY IMMUNIZING A CHILD



Source: UNICEF, WHO

To highlight increased complexity, WHO recommends regional vaccines targeting sub-Saharan Africa and Asia. In Africa, the vaccine recommendations in some regions would include yellow fever, MenA, and typhoid, as well as others, and soon the malaria vaccine will be added. This increases the number of vaccines and the number of doses per child for the three diseases: meningitis, typhoid, and yellow fever. To fully immunize a child in sub-Saharan Africa with the full EPI schedule of vaccines, including the three current regional vaccines, brings the total number of vaccines to 11 for 14 antigens, requiring 24 doses per child.

34 MSF, *The Right Shot: Extending The Reach of Affordable and Adaptable Vaccines: 1st Ed*, p. 3.
35 In 2001, UNICEF purchased pentavalent for $3.50 a dose, or $10.50 for the three recommended doses. When added together with BCG, OPV and measles vaccines, the total cost to fully vaccinate a child was $11.63.
36 World Health Organization, *WHO Recommendations for Routine Immunization - Summary Tables*, WHO, Geneva, November 2021.
37 UNICEF, *Pricing Data*, UNICEF, Copenhagen, February 2023.

Emerging adolescent and adult immunization with COVID-19, HPV, and Td further increases the number of vaccines and doses. These recommendations exclude any emergency outbreak responses to infectious diseases such as cholera or Ebola, amongst many others.

Thanks to innovations, additional vaccines are now available to improve the lives of children. As new antigens are developed, immunization programmes will increase further over time and complexity as life course immunization schedules expand. Simplifying child immunization programmes will require more combination vaccines to reduce the immunization burden on health systems, as well as the touch points a child needs to have with health facilities. Even though there are positive considerations to be had by increasing the number of visits a child pays to health facilities, as well as to catch up on missed doses, there are also considerations to be had for the burden on families especially the poorest. Immunization partners are working on how to ease systems of vaccine delivery and methods of administration to reduce the demand for immunization devices (e.g., syringes and safety boxes) with innovative solutions such as using microarray patches and possibly jet injectors. A key consideration will be the need to ensure immunization equity and how the system evolves and expands to include additional immunization during adolescents and adulthood, as a life course of immunization expands to vaccines such as COVID-19, HPV, and maternal tetanus.

There is also an increased level of attention and growing concern over the risk of emergency outbreaks following the consequences of COVID-19, which call for considerable efforts to build back better and improve pandemic preparedness and response. New vaccines will incur high costs for some antigens and will increase the complexity of immunization programmes, for example, if new vaccines have new cold chain requirements. The most significant market-shaping gains have been achieved through the introduction of new and underused vaccines, price reductions, and vaccine product innovation. However, additional market shaping opportunities still exist, for example, targeting vaccines for HIV, malaria, and TB, amongst others, as well as improving vaccine presentations to reduce the number of doses a child requires as well as offering a longer shelf-life, ease of administration, broader protection, and lower carbon footprints.

3.4 Overcoming immunization programme obstacles

Vaccine-related innovations have the potential to address some of the existing barriers to immunization and are urgently needed to achieve equitable vaccine coverage as articulated in the World Health Assembly's Immunization Agenda 2030.[38] So far, most recent vaccine innovations have helped solve supply chain-related obstacles, such as tracking shelf-life, preventing temperature excursions, preventing needle stick injury and needle reuse. Very few innovations have been aimed at vaccine products overcoming immunization inequity. Opportunities exist to address the growing areas of immunization complexity to ensure that pricing remains affordable, with additional combination vaccines and scheduling optimization to reduce vaccine visits, for example, through thermostable vaccines, requiring less refrigeration to reach children outside the cold chain.

The Vaccine Innovation Prioritisation Strategy (VIPS)[39] is a collaboration between UNICEF, BMGF, Gavi, PATH, and WHO to develop a single integrated framework to evaluate and prioritize vaccine product innovations. In 2020, VIPS prioritized a number of innovations to be explored further, notably: i) microarray patches (MAPS) that will, in the future, allow administration of a vaccine dosage through the skin; ii) heat-stable and controlled temperature chain-enabled liquid vaccine formulations that will allow vaccine coverage to increase beyond the reach and confines of a cold chain; and iii) potential benefits of using barcodes on primary packaging. UNICEF and its partners are prioritizing these innovations to overcome the challenges of delivering vaccines to resource-limited contexts and reaching zero-dose children. In addition, these innovations already have a good level of technical readiness and are commercially feasible.[40] As of January 2022, UNICEF has been implementing a requirement for barcodes on the secondary packaging of vaccines to help facilitate track and trace, improve stock management, and identify falsified and substandard vaccines.

38 WHO, *Immunization Agenda 2030: A Global Strategy to Leave No One Behind.*

39 World Health Organization, *Product Development for Vaccines Advisory Committee Executive summary 2020: The Vaccine Innovation Prioritisation Strategy (VIPS)*, WHO, Geneva, July 2020.

40 Giersing, Birgitte, Natasha Shah, Debra Kristensen, et al., *Strategies for Vaccine-product Innovation: Creating an Enabling Environment for Product Development to Uptake in Low- and Middle-income Countries*, Elsevier, Vaccine, Volume 9, Issue 49, Amsterdam, December 2021, p. 7208-7219.

Staff from Nigeria's National Agency for Food & Drug Administration and Control use barcode technology to verify the authenticity of a vaccine consignment at the medical warehouse.

3.5 Innovations in manufacturing

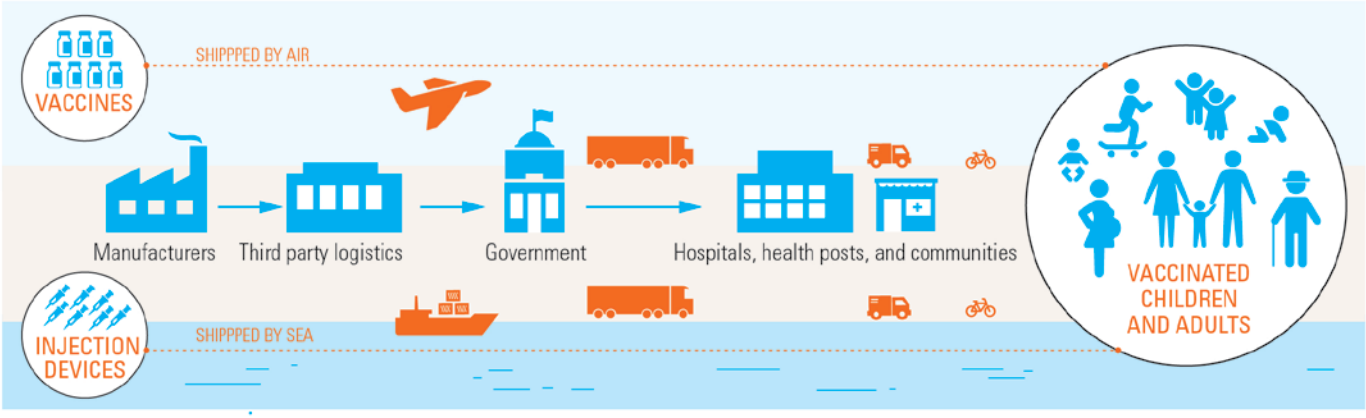
UNICEF welcomes other manufacturing innovations, such as platform technologies enabled by investments by partners such as CEPI and BMGF, as well as WHO's technology transfer hub and spoke programme in South Africa to build the capacity of African manufacturers to develop and produce vaccines based on the mRNA technology.[41] It also supports small footprint, lower cost, scalable, modular, manufacturing facilities; upstream supply chain solutions, including market dashboards for matchmaking by CEPI. CEPI also launched the 100-day manufacturing vision to strive for the development and access to a safe and effective vaccine against pandemic pathogens in 100 days, as well as manufacturing at scale through networks.

3.6 Strengthening the vaccine logistics through digital technology

UNICEF also supports supply chain system innovations. Besides using ViVa online stock projection dashboard that visualizes the pipeline of vaccine orders and forecasts as well as the stock levels under certain demand scenarios, UNICEF also pilots with partners to enable the track and trace of vaccines via the traceability and verification system (TRVST).[42] The availability of barcodes on vaccines will have the potential to increase supply chain efficiencies, inventory management, and reduce processing times and administration, including eventually facilitating electronic immunization cards and coverage monitoring. It will ensure that the rights of patients are secured by protecting patient safety through identifying falsified and substandard vaccines, and by ensuring children and adults get the right vaccine at the right time.

41 World Health Organization, *The mRNA Vaccine Technology Transfer Hub*, WHO, Geneva, June 2021.
42 UNICEF, *Track and Trace of Vaccines*, UNICEF, Copenhagen, 2022.

Figure 12: THE SUPPLY CHAIN IN DELIVERING VACCINES



Suppliers will benefit by accessing the markets and protecting their brands from misuse and falsification, simplified data, and interoperability. The system also has the potential for countries, when fully implemented, to help with product verification, improved inventory management avoiding stock outs and allow for optimal use of available stocks based on shelf-life, enable recalls, and help capture better administrative data, including patient data accuracy.

TRVST will link with the electronic logistics management information system (eLMIS) with Gavi support, which is a revolutionary, cost-effective health data management system to ensure that health facilities are linked to their central stores to collect and distribute logistics data in real time. Digital technology has the potential to create a more operational management system, which enables countries to use data and link it to their eLMIS, which is a closed country system, to help manage inventories, process orders and move stock.[43]

3.7 Outlook for cold chain equipment

Despite a tenfold increase in spending on vaccines to fully immunize children, additional requirements in terms of antigens, doses, clinical visits, and a global target population size that has doubled from 4 billion in 1974 to 8 billion in 2023, advances in cold chains systems have not been benefitting from a commensurate level of funding, investment, or interest. National cold chain inventories in many locations were found to be ageing, underperforming, or were no longer considered optimal, or unusable in locations that had no reliable electricity. Designed in the 1980s, they were straining to cope effectively with the increase in storage capacity requirements to reach populations that had yet to access immunization services.

UNICEF and Gavi have been collaborating since 2017 to improve countries' cold chain capacity and address several critical issues. In terms of funding, cold chain equipment was often insufficient or not sufficiently budgeted to meet a country's full extent of requirements. Whereas some countries had difficulty purchasing new higher performing cold chain equipment technologies, the up-front capital investments could often be far higher for new replacement technologies, despite an overall lower estimated total cost of ownership during its life cycle. Many countries lacked a proper inventory system, which prevented them from clearly understanding their cold chain equipment gap requirements to accommodate the necessary vaccine storage volumes at various levels of their supply chain.

Countries also often did not have sufficient information to compare the different available equipment options, as well as to understand their associated lifetime operating costs, durability, and sustainability in field conditions. The cold chain equipment market also had several shortcomings, notably its limited visibility on global demand requirements. The supply side of the market was very fragmented, and the procurement was equally as fragmented, with pricing being very unclear. Until recently,

43 Centre for Health Market Innovations, *Electronic Logistics Management Information System (eLMIS)*, CHMI, Washington, 2022.

there were also very few incentives to adopt more appropriate and innovative technologies. A critical requirement was a need for information exchange through regular industry consultations and demand forecasts, whereby information could be exchanged and communicated between suppliers, procurement agents, and countries so that all could be better informed on the best product choices.

UNICEF and Gavi address these challenges through health systems strengthening (HSS) and funding to support eligible LICs to invest in cold chain systems and to assist them scale-up vaccine introductions and cold chain equipment procurement.

The Cold Chain Equipment Optimization Platform (CCEOP) offers unique funding opportunities for eligible countries to procure technologies that optimize vaccine delivery and storage, and safeguard vaccine potency.[44] It also addresses market challenges through market shaping, which includes informing country choices and suppliers and the visibility of products on offer and in demand, as any production and procurement planning is complex. Between 2018 and 2022, under the CCEOP, 68,000 vaccine refrigerators with a combined storage capacity of nearly 4,500 m3 were procured, delivered, and installed at health facilities in 49 countries, increasing access to vaccines in hard-to-reach communities, including through solar technology in unelectrified places and replacing kerosene refrigeration systems. Between 2018 and 2022, UNICEF procured 120,000 vaccine refrigerators with a combined storage capacity of 12,000 m^3 and were installed at health facilities in 122 countries.

From 2002 to 2016, funding for cold chain equipment averaged approximately $22.5 million a year. Through CCEOP and with Gavi's support, funding for cold chain equipment increased to approximately $100 million a year and was especially focused on strengthening vaccine supply chains to reach the 'last mile' and children living in remote areas. Through cold chain partnerships, UNICEF procured battery-free solar-powered fridges, which are critical for vaccinations in areas with unreliable electricity. Over 2021 and 2022, funding for cold chains reached approximately $200 million a year as a

44 Gavi, the Vaccine Alliance, *Cold Chain Equipment Optimization Platform: The Technology Guide*, Gavi, Geneva, February 2022.

UNICEF and the Government of Japan partnered with the Government of Uganda to support the enhancement of cold chain capacity and or increase the vaccine storage capacity in the country. © UNICEF/Abdul

result of the COVID-19 pandemic, which provided a unique opportunity for countries to invest in increasing vaccine storage capacity at national and sub-national levels. Countries procured cold chain equipment with larger storage capacity via various new funding modalities. COVAX made $50 million available for the procurement of cold chain equipment by 74 participating countries. The Government of Japan provided significant investment reaching over $100 million. The World Bank and the COVID-19 vaccine delivery support, with funding by Gavi, provided additional support for cold chain equipment. Other donors, notably USAID and Germany, also contributed substantial resources for cold chain equipment procurement. In 2022, UNICEF provided an additional 7.4 million litres of cold chain equipment storage capacity to over 104 countries.

Whereas most vaccines need to be maintained under strict temperature control conditions between 2°C and 8°C, some of the new vaccines against Ebola and COVID-19 require ultra-cold chain equipment that controls temperature between -60°C to -80°C. Funding availability from partners in response to the COVID-19 pandemic allowed UNICEF to equip over 70 countries with well-functioning freezers capable of storing these vaccines safely. Additional new funding is now available for African countries via the collaboration between Africa Centres for Disease Control and Prevention (Africa CDC) and the Mastercard Foundation to build resilience and preparedness for future pandemics.

Cold chain technologies being made available through UNICEF and supported by BMGF, the Clinton Health Access Initiative (CHAI), Gavi, WHO, and the World Bank include:[45]

See Figure 13 on next page

UNICEF also supports the development of solar-powered cold rooms allowing countries to store larger volumes of vaccine in areas without regular mains power supply and refrigerated vehicles that could transport larger volumes of vaccine without the need to repack them in cold boxes and vaccine carriers. This equipment will help update the standard and quality of cold chain systems to allow immunization activities to reach communities through more touch points and create opportunities for UNICEF to increase cold chain capacity in countries.

45 Ibid.

Figure 13: COLD CHAIN EQUIPMENT PRODUCTS USED IN IMMUNIZATION

On-grid freezers designed to have better temperature control and reliability than standard domestic freezers.

Ice-lined refrigerators (ILRs) designed with longer holdover times to keep vaccines cool during prolonged periods of power outage (more than two days). Ice-lined refrigerators models require only eight hours of power per day to keep vaccines within the required temperature between 2°C and 8°C.

Remote temperature monitoring devices (RTMDs) capable to continuously record temperature and transmit the data to a central location for recording and monitoring purposes.

Solar direct drive (SDD) refrigerators and freezers that run on solar power, battery free, requiring less maintenance, and can come with integrated energy harvesting control (EHC), which allows extra solar power to be available for a variety of uses at the health facility, including charging cell phones, laptops, radios, and battery-powered lanterns, or power devices such as RTMDs, fans, and lighting.

INNOVATIVE TECHNOLOGY MADE AVAILABLE THROUGH UNICEF

30-day temperature recorders (30-DTRs) with five-year battery life that log temperatures for one month periods and indicates alarms in case of temperature excursions to health care providers locally.

Long-term passive storage devices designed to keep vaccines cold for long periods without any source of power and that do not require direct solar panels, batteries, electricity, gas, or other fuels.

Insulated freeze-preventive cold boxes and vaccine carriers used to transport vaccines between facilities or during field immunization sessions. They prevent freeze damage to vaccines and do not require user intervention such as ice pack preconditioning, saving time when preparing vaccines for transport.

Extended voltage stabilizers protect refrigerators and freezers powered by mains electricity from damage caused by extreme fluctuations in the electricity supply and voltage and frequency levels that are either too low or too high for reliable functioning, as from lightning strikes.

Soon there will be next generation Equipment Monitoring Systems (EMS), which monitor more aspects of cold chain equipment performance than temperature.

Environmental considerations: All refrigerators supplied by UNICEF use only refrigerant gases with zero ozone depletion capability thus not contributing to global warming.

Auxiliary nursing midwives Beauty Bolo Roy, left and Parmeswari Adhikary, centre, along with a social health activist, taking a 2 hour boat ride to reach Fulkakata village to conduct nutrition day visits, on December 7, 2022 in Dhubri district, Assam, India. UNICEF supplied vaccine carriers to the District Health Teams to preserve the cold chain for the vaccines. © UNICEF/Baruah

4. A look forward

In terms of future developments in vaccine markets, UNICEF identifies a number of priority areas for new pipeline vaccines and related areas that can significantly impact children and immunization programmes. Working with strong global health partners, donors, countries, and the private sector, UNICEF aims to address equitable access to vaccines by focusing on opportunities to expand research and development to:

- Develop additional combination vaccines, such as the work UNICEF partners are already engaged in developing a hexavalent vaccine,
- Develop and bring new antigens to market, which is critical in the context of public health emergency preparedness against new and recurring outbreaks against which there is no protection,
- Achieve sustainable, affordable pricing,
- Facilitate vaccine administration and delivery,
- Extend vaccine shelf-life,
- Offer longer protection,
- Improve thermostability,
- Address environmental considerations.

These all offer opportunities to further expand research and development. UNICEF and partners are already targeting focused engagement in the hexavalent vaccine and number of vaccine products related to HIV, HPV, malaria, and TB.

4.1 Hexavalent vaccine

New combination vaccines have the potential to increase universal immunization coverage and save costs by providing a full life course of vaccines with fewer injections administered per child, reducing the number of touch points between the child and health facilities, and having fewer vaccines to keep stocked. As such, the hexavalent vaccine is a good example of a combination vaccine that can potentially achieve these advantages. The hexavalent vaccine combines the five antigens of the pentavalent vaccine with IPV. While it is to be procured through UNICEF and funded by Gavi for eligible countries, this new vaccine will need to demonstrate commensurate economic value to replace the cost to immunize with a schedule of three doses of pentavalent, two doses of IPV for primary series, and a DTP booster in the second year of life.

Any new vaccine will need to show a significant impact on the cost burden for LICs, as new vaccines are by their nature more expensive, given the level of technology, innovation, and resources required in their development, and which need to be recovered through reaching economies of scale once introductions are achieved.

One of the key challenges UNICEF and its partners will have in their approach to hexavalent vaccine procurement is the management of its supply of bulk. Bulk is the vaccine's substance, which is the main ingredient of the biological product. The same source of bulk is used to produce the other DTP- HepB- Hib- and IPV-containing vaccines. Bulk is in limited supply, so it must be carefully planned and shared between the different products to ensure they all remain available. As with previous similar UNICEF and partner collaboration on scaling up the use of pentavalent vaccines, securing affordable and sustainable access to hexavalent vaccine supply will need to be balanced against simultaneously maintaining the healthy markets for pentavalent and IPV standalone vaccines. UNICEF and partners will continue to have a critical role in ensuring and maintaining a healthy market for all IPV-, DTP-, HepB-, and Hib-containing vaccines.

4.2 HIV vaccine

HIV and AIDS remain a global public health challenge and are responsible for over 40 million deaths since the start of the epidemic in 1981. As of 2021, approximately 38.4 million people were globally living with HIV/AIDS. To reach the new proposed global 95–95–95 targets set by UNAIDS, programmes need to redouble efforts to avoid 7.7 million HIV-related deaths over the next ten years, which is set against an increased HIV infection rate due to HIV service disruptions during COVID-19, and the slowing public health response to HIV.[46] Just under 70 per cent of people living with HIV are in Africa, a region that accounts for 91 per cent of all children living with HIV/AIDS and 85 per cent of all adolescents worldwide. Each day 1,780 people die from HIV-related causes, mostly because of inadequate access to HIV prevention, care, and treatment services. An effective, or even a partially effective vaccine could decrease the number of people

46 World Health Organization, *HIV, Key Facts*, WHO, Geneva, November 2022.

who acquire HIV, further reducing the number of people who can pass the virus on to others. The most recent large-scale HIV vaccine trial was found to be safe, but it did not provide protection against HIV acquisition and other concepts are being studied.[47] Even though there will not be any HIV vaccine available in the near term, there are early-stage experimental product trials underway.

4.3 HPV vaccine

The HPV vaccine protects against cervical cancer, the second most common cancer in women. Every year, an estimated 342,000 women die from cervical cancer, of which more than 90 per cent of deaths are in LICs and MICs. It is one of the most cost-effective vaccines in terms of lives saved. Global HPV vaccination coverage of the first dose (HPV1) was 15 per cent in 2021, having declined by 25 per cent from 2019,[48] and second dose coverage (HPV2) decreased from 14 per cent in 2019 to 12 per cent in 2021. So globally, over a quarter of the coverage of HPV vaccines achieved in 2019 has been lost. Low global HPV coverage is driven by a number of issues, notably delayed national introductions due to competing vaccine priorities, vaccine supply shortages, the high cost of the vaccine, and demand complexities, including those driven by gender-related barriers as well as school closures due to the COVID-19 pandemic. In the last five years, global HPV vaccine supply availability has also been insufficient to meet the demand, and consequently, the HPV vaccine market has been constrained and not sufficient to meet the increased requirements. As a result, countries introducing the vaccine with the support of Gavi had to postpone their vaccination plans. Self-financing MICs seeking supply through UNICEF were also unable to access sufficient supply.

Even though school-based vaccination can achieve high coverage of girls and boys, it could incur high costs, and as such, there is a need for investments. Due to the unique target age and gender group, there are complexities around demand generation and establishing trust for HPV vaccination in local communities. There is a need for investments in community engagement to address vaccine hesitancy. HPV vaccination has been one of the most disrupted immunization programmes due to COVID-19. The HPV vaccines are delivered through a mix of activities and strategies using schools, health facilities, and community outreach in countries to ensure that immunization programmes reach all adolescent girls, especially those out of school who are especially vulnerable. The closure of schools and health facilities reduced EPI capacity due to the redeployment of health workers and the restrictions placed on population movements which contributed to the decline in HPV coverage.

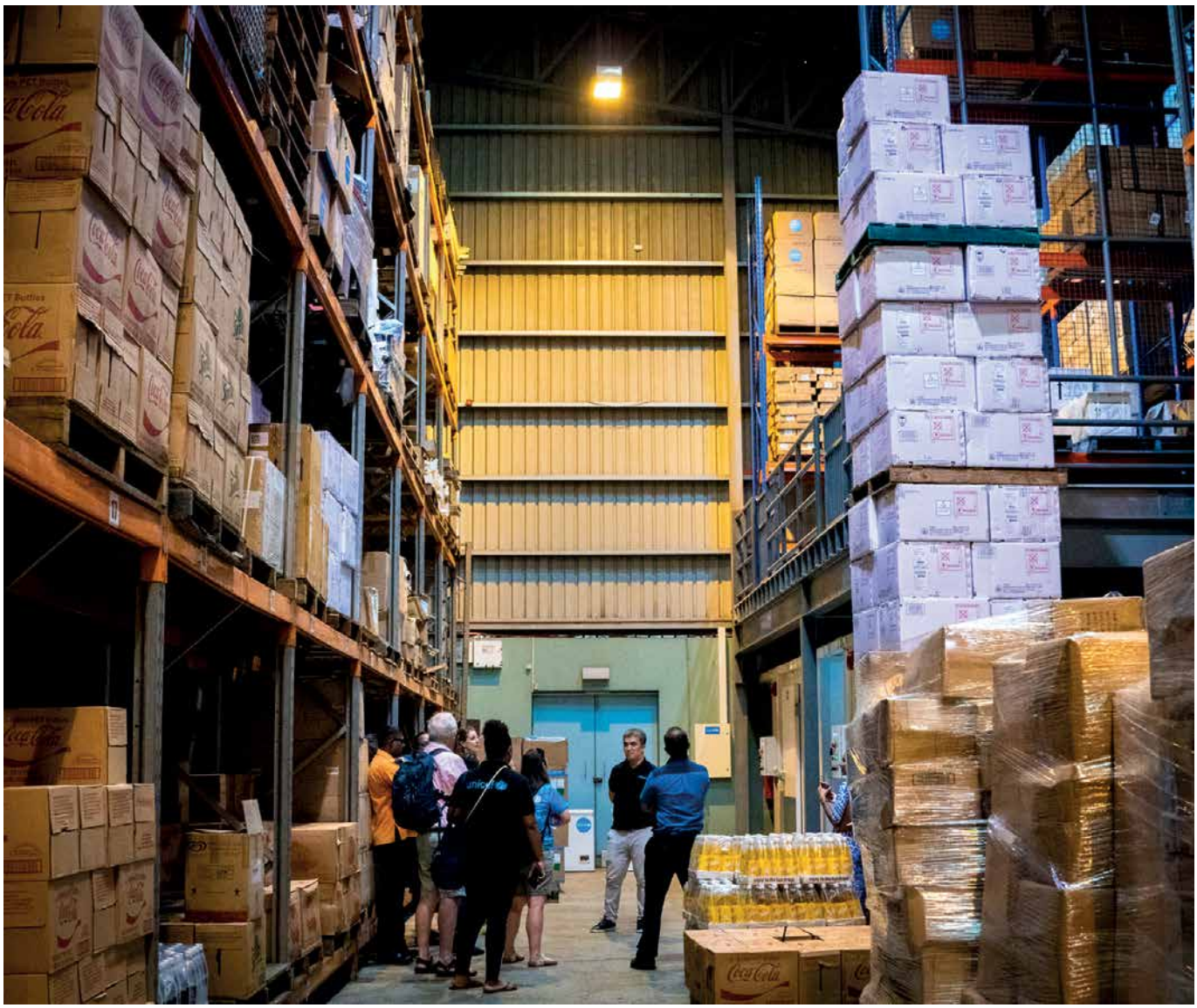
Supply availability is improving with increased production capacity among existing suppliers and WHO's prequalification of a new HPV bivalent vaccine in 2021. Supply will need careful planning for countries supported by Gavi until 2024, depending on the timing of large multi-age cohort (MAC) vaccination, product choice, and schedule decisions.

HPV vaccine pricing also remains high and varies significantly between different country income levels. Vaccine affordability is a concern for most self-financing MICs considering HPV introduction, as well as for many Gavi-supported countries seeking to sustain HPV vaccination once they transition from Gavi support and self-finance their HPV procurement. Strong and sustained HPV vaccination programmes, along with improved screening and treatment, are the only affordable way to reduce HPV cases and prevent deaths from cervical cancer now and in the future, especially for women in LICs and LMICs.

4.4 Malaria vaccine

Currently, malaria is responsible for an estimated 247 million cases a year, and kills an estimated 619,000 people, of which Africa carries a disproportionate share of the burden.[49] After 35 years of product development, WHO recently approved the first vaccine against malaria

47 HIV Gov, *HIV Vaccine Research Update with Dr. Dieffenbach from CROI 2023*, HIV Gov, Washington, February 2023.
48 World Health Organization, *WHO Updates Recommendations on HPV Vaccination Schedule*, WHO, Geneva, December 2022.
49 World Health Organization, *Malaria, Key Facts*, WHO, Geneva, March 2023.



In October 2022, UNICEF Australia and Rotary teams visit the UNICEF Pacific supply warehouse in Nadi, Fiji. The Rotary and UNICEF partnership is delivering pneumococcal conjugate vaccine (PCV), rotavirus vaccine (RV), and the human papillomavirus vaccine (HPV) to protect children and adolescents. © UNICEF/Labade

targeting children living in areas with moderate to high malaria transmission.[50] It currently requires a four-dose schedule outside the EPI schedule, which implies significant programmatic implications and costs. It is currently in limited supply while progress is made towards the convergence, balance, and alignment between country demand and production scale up. UNICEF currently expects the malaria vaccine supply to be constrained over the next two to five years. It anticipates the market to meet expected demand sometime between 2026 and 2028, depending on the successful scale-up of the vaccine's production. UNICEF anticipates accessing the first WHO-prequalified malaria vaccine as of late 2023 and 2024, with additional supply increasing over 2025 and beyond. To help ensure the malaria vaccine's long-term sustainable supply, accessibility, and affordability, the manufacturer, with the support of PATH, will transfer vaccine technology in manufacturing the antigen to another supplier with greater production capacity, thereby increasing supply and speeding up availability. The malaria vaccine's currently anticipated high price at EUR 37.00 per course reflects that production is not yet at a steady state or benefitting from economies of scale. Other malaria vaccine products are in the final stages of trials prior to approval and WHO policy recommendation and prequalification.

50 World Health Organization, *WHO Recommends Ground-breaking Malaria Vaccine for Children at Risk*, WHO, Geneva, October 2021.

4.5 BCG vaccine

A total of 1.6 million people died from TB in 2021, including 187,000 people with HIV.[51] The vaccine against TB was developed 100 years ago and was first used in 1921. It is one of the world's most widely used vaccines,[52] and has been part of the EPI since the programme's initiation in 1974. BCG vaccines have historically had a solid supply base and are effective in preventing TB in infants. It is a vaccine recommended at birth in countries or settings with a high incidence of TB and leprosy, ideally administered together with a dose of HepB. However, BCG vaccines have limited effectiveness in older age groups, and in addition, the protection offered has not been consistent against all strains of TB in all age groups.[53]

Much more effective TB vaccines are needed to decrease TB mortality,[54] particularly to prevent pulmonary TB, the most common form of the disease. Pulmonary TB mostly occurs in adolescents and adults and is responsible for TB transmission. Considerable efforts are being made by international donors, manufacturers, and research institutions to develop second generation TB vaccines using different technologies. Several next generation TB vaccine candidates are currently in advanced stages of clinical development and studies. Whereas some pipeline products are designed for use as a booster dose following primary neonatal BCG vaccination, others are being evaluated for use in adolescents, adults, and in therapy.

According to the TuBerculosis Vaccine Initiative (TBVI), there are 22 different TB candidate vaccines undergoing different stages of development.[55] Researchers are investigating the effectiveness of these new TB vaccines to see if any can equally be used to prevent TB in infants, adolescents, and adults, prevent latent TB from becoming active, as well as treat active TB, and prevent transmission. Researchers made some advancements in the prevention of active pulmonary TB disease in adults, notably in the positive clinical trial outcome of one product vaccine.[56] However, there is currently no information on when new vaccines will be available.

51 World Health Organization, *Tuberculosis, Key Facts*, WHO, Geneva, April 2023.
52 Hansen-Flaschen, John, *BCG Vaccine*, Encyclopaedia Britannica, 2018.
53 World Health Organization, *BCG Vaccines: WHO Position Paper*, WHO, Geneva, February 2018, p. 84.
54 World Health Organization, *Global Tuberculosis Report*, WHO, Geneva, October 2022, p. 159.
55 The TuBerculosis Vaccine Initiative, *Pipeline of Vaccines*, TBVI, Lelystad, October 2022.
56 Aeras, *Advancing TB Vaccine Science*, Aeras, Cape Town, 2019.

Rhoda Joshua, in charge of Fufore Primary Health Centre in Nigeria, is holding the box of Rectal Artesunate and patients referral booklet. Rectal Artesunate is a pre-referral intervention administer to children under 6 years to reduce the chance of death and enduring disability by about 50 per cent. It serves as a stopgap treatment for children with severe malaria before making a referral to the appropriate health facilities. © UNICEF/Esiebo

A midwife at a UNICEF primary healthcare centre opens a mosquito net from a Mama-baby Kit for new mother Nurjahan and her newborn. © UNICEF/Sujan

4.6 Climate change

The environment and climate are factors that significantly influence all diseases, including vector-borne diseases, which are responsible for so many viruses. These vectors, such as mosquitoes, fleas, and ticks, amongst many others, are living organisms that carry and transmit infectious pathogens to other living organisms and are heavily influenced by seasonality and environmental and climate changes year to year. Climate change variability is a factor leading to changes in how vectors and pathogens adapt. Out of all vectors, mosquitoes are responsible for transmitting more diseases than any other. They transmit chikungunya, dengue fever, Japanese encephalitis, malaria, Rift Valley fever, West Nile virus, yellow fever, and Zika, amongst others.[57]

An. stephensi is a mosquito species native to south Asia and parts of the Arabian Peninsula. It can transmit both P. falciparum and P. vivax malaria parasites. Over the past decades, it has been spreading across Africa, having been detected in Djibouti (2012), Ethiopia and Sudan (2016), Somalia (2019) and Nigeria (2020).[58] It thrives in urban settings and has been found to be resistant to many insecticides used in public health control measures, which poses an added challenge to its control. The spread of this mosquito across a region where the burden of malaria is highest is particularly worrying and is thought to have contributed to a resurgence of malaria in Djibouti and at least one outbreak in Ethiopia.

57 World Health Organization, *Vector-borne Diseases*, WHO, Geneva, March 2020.
58 World Health Organization, *World Malaria Report 2022*, WHO, Geneva, December 2022, p 6.

Changes in climate and epidemiology are compelling epidemiologists and product developers to include the effect of changing climatic variables in future intervention strategies.[59] For example, yellow fever is endemic in tropical areas of Africa and Latin America, home to an aggregate at-risk population of over 900 million people, and has been increasing in incidence. Over the last two decades, it has been infesting regions from which it was previously eliminated.[60] Shifts or expansions in geographic range change disease incidence and can affect host immunity, as well as the mutation of the pathogen, as with flu, and as seen with COVID-19, as with Ebola. Some experts identify that over half of known human pathogenic diseases can be aggravated by climate change.[61]

4.7 Public health emergency preparedness, research, and development

WHO has a research and development (R&D) blueprint for epidemics. It targets R&D on diseases that present the greatest threat of an epidemic or pandemic outbreak, with the objective of strengthening global preparedness and response measures. Its R&D blueprint serves to accelerate product development for priority antigens before they emerge, so as to shorten the timeline necessary to develop safe and effective diagnostics, treatments, and vaccines. The last prioritization exercise WHO conducted was in 2018. WHO expects to release its latest updated prioritization exercise in 2023, following the lessons it has learned from COVID-19. The R&D blueprint adopts a viral family approach to identifying viruses, as it offers a framework to fast-track research and encourages research efforts on entire classes of viruses, instead of just individual strains, so as to improve the capability to respond to unforeseen strains, zoonotic viruses, and as yet any unknown disease.[62]

The current R&D roadmaps target the accelerated development of products for Ebola, Marburg, Crimean-Congo haemorrhagic fever, Lassa fever, Nipah virus, and Zika virus. An R&D roadmap for Rift Valley fever is currently in development with the Food and Agricultural Organization (FAO), the World Organization for Animal Health (WOAH), and WHO.[63]

Rift Valley fever is a viral disease most commonly seen in domesticated animals in sub-Saharan Africa and is transmissible to people through contact with infected body fluids or bites from infected mosquitoes. Over the last 20 years, there have been 14 outbreaks across Africa, meaning an outbreak every year, if not every other year.[64] Whereas most cases show no or only mild symptoms, some can develop haemorrhages (excessive bleeding) and encephalitis (swelling of the brain).

Downstream, UNICEF has been working with global health partners and governments to prepare for, and respond to, public health emergency outbreaks involving infectious diseases, whether nationally, regionally, or globally. Preventing and responding to public health emergencies requires a full range of coordinated and complementary measures across multiple sectors to protect children and their families. UNICEF efforts have focused on the procurement of emergency vaccines and supporting the implementation of immunization programmes involving the community, which combines risk communication, community engagement, and behavioural change. Programme interventions cover water, sanitation and hygiene (WASH), including vector control and the provision of clean water for infection prevention and control (IPC) in health facilities and at community level. UNICEF and partners support government-led national, community, and primary health systems to enhance community-based surveillance, contact tracing and isolating suspected cases, together with the procurement of supplies for outbreak response programmes. Innovative approaches are also needed for mental and psychosocial support that contribute to enabling people's participation in an

59 Gaythorpe Katy, Hamlet Arran, Cibrelus Laurence, et al., *The Effect of Climate Change on Yellow Fever Disease Burden in Africa*, PubMed, Bethesda, July 2020.
60 World Health Organization, *Vaccines and Vaccination against Yellow Fever, WHO Position Paper*, WHO, Geneva, June 2013, p. 271.
61 Mora, Camilo, Tristan McKenzie, Isabella M. Gaw, et al., *Over Half of Known Human Pathogenic Diseases Can Be Aggravated by Climate Change*, Nature Climate Change, London, August 2022.
62 World Health Organization, *WHO R&D Blueprint for Epidemics: Targeting Research on Diseases of Greatest Epidemic and Pandemic Threat*, WHO, Geneva, February 2023.
63 World Health Organization, *Rift Valley fever, Key Facts*, WHO, Geneva, February 2018.
64 Centers for Disease Control and Prevention, *Rift Valley Fever Outbreak Summary*, CDC, Atlanta, February 2020.

Aurobinda Parida, the district vaccine and logistic manager of Rayagada district vaccine store, is showing the vaccine stock register to Joshila Pallapti of UNICEF. Rayagada DVS is first ISO 9001:2015 certified DVS in Odisha. © UNICEF/Ghosh

effective response while minimizing its impact in their mental health. The development and implementation of costed national action plans for health security (NAPHS), the foundation at country level for better epidemic preparedness and response, is a cornerstone of these efforts, as well UNICEF's public health emergency teams.

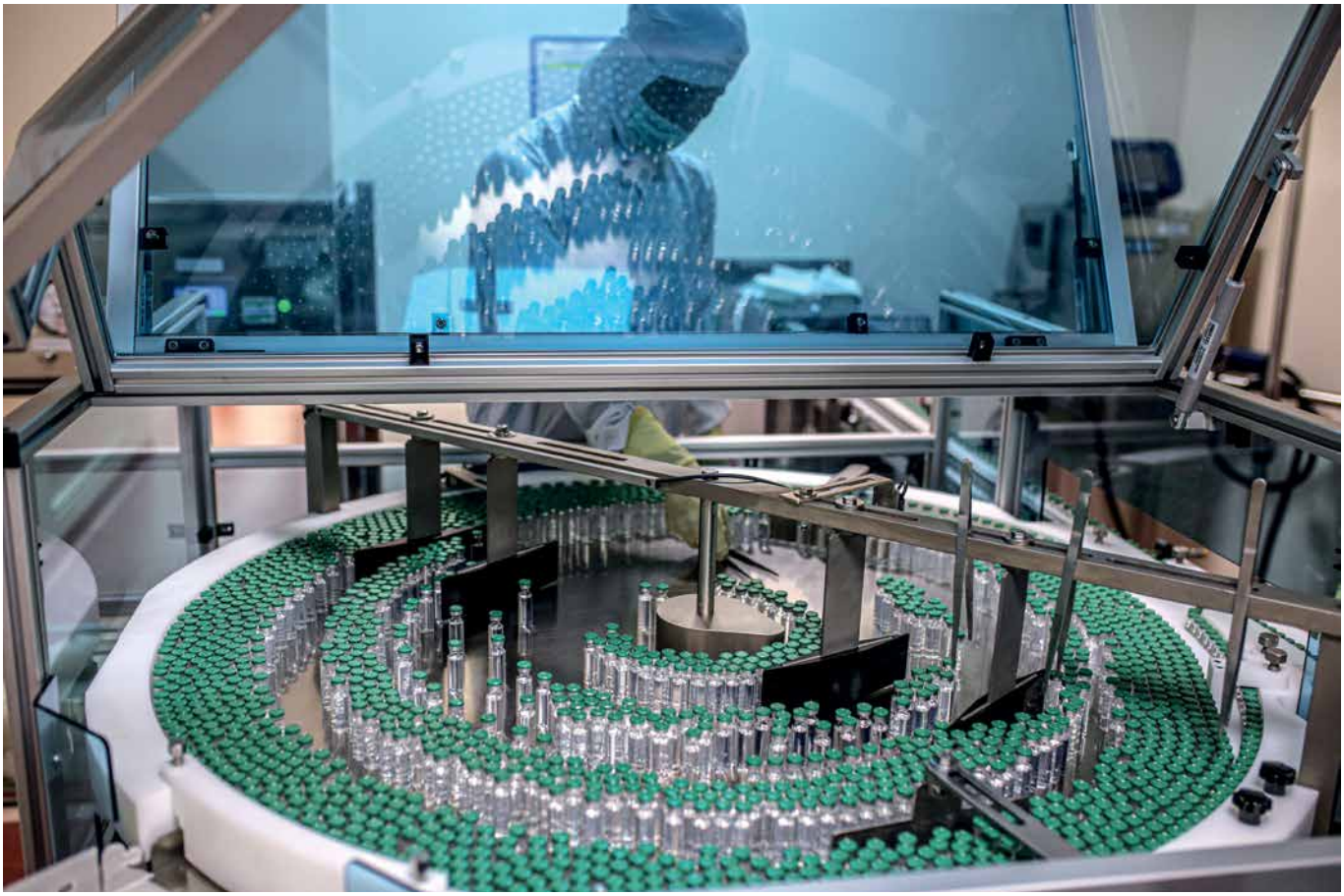
UNICEF's Strategic Plan for 2022-2025 complements UNICEF's Health Strategic Plan for 2022 - 2025 in identifying and covering the unreached with life-saving vaccines, other health products, and care for all.[65] This will require health agencies to work together to eliminate gaps in surveillance, testing and sequencing to understand how viruses change, gaps in vaccination to reduce the risk of vaccine preventable disease incidence and mortality, gaps in treatment to prevent unnecessary deaths, gaps in health systems to ensure it can cope with the holistic treatment of patients, and gaps in knowledge to better understand how best to prevent, prepare and respond to the outbreak of infections. It will also focus on strengthening public health emergency preparedness and response strategies.

4.8 Investing in vaccine development

There is a significant productivity gap in vaccine development, referring to the resources directed towards product R&D and the resulting number of market-approved products. Some research estimates that product development takes on average 11.9 years and an investment around $0.8 billion to launch one product on the market, and only 22 per cent of candidates successfully complete clinical testing. However, there are candidate success rates which range from 7 per cent to 78 per cent, and investments ranging from $0.8 to $1.7 billion.[66]

The cost of developing a vaccine against an

65 UNICEF, *UNICEF Strategic Plan 2022–2025 Renewed Ambition towards 2030*, UNICEF, New York, January 2022, p. 11.
66 Pronker, E.S., T.C. Weenen, H.R. Commandeur, et al., *The Gold Industry Standard for Risk and Cost of Drug and Vaccine Development Revisited*, Vaccine Vol. 29 Issue 35, Amsterdam, June 2011.



An employee works on the production line of a COVID-19 vaccine manufacturer for the COVAX facility in Pune, Maharashtra, India.
© UNICEF/Dhiraj Singh

epidemic infectious disease from preclinical trials through to end of phase 2a[67] is estimated to reach $31 to $68 million, assuming success. Between 11 to 21 preclinical candidates would be required if at least one vaccine were to progress through to end of phase 2a. Starting from phase 2, the average cost of successfully advancing at least one vaccine through to the end of phase 2a can reach between $84 to $112 million, and between $319 to $469 million from preclinical, and includes the cost of failed vaccine candidates. Progressing one of these vaccines through to the end of phase 2a for each of the candidates would cost a minimum of $2.8 to $3.7 billion.[68]

Other research estimates that between $12.7 billion and $18.7 billion should be spent on developing 40 vaccine candidates for potential epidemic diseases, including testing in phase 2 clinical trials. This serves to highlight that developing a vaccine is expensive, and that there is a need to sustain the investment in vaccine development, and engagement in immunization activities. However, the massive global investment and collaboration in response to COVID-19 demonstrated what incredible achievements can be reached in such a short time - providing from scratch, almost two billion vaccines to 146 countries and territories.

4.9 Sustainable procurement

Even though many of the targets set by the Decade of Vaccines (2010 to 2020) have not been met, substantial progress has been made.[69] The greatest impact has been on the reduction in global under-five mortality as a result of vaccine introductions and the scale up of underused vaccines across the majority of countries. Coverage goals were not all

67 World Health Organization, *How are Vaccines Developed?*, WHO, Geneva, December 2020.
68 Gouglas, Dimitrios MSc, Tung Thanh Le MSc, Klara Henderson PhD, et al. *Estimating the Cost of Vaccine Development against Epidemic Infectious Diseases*, The Lancet Global Health, London, October 2018.
69 MacDonald, Noni, Mohsni Ezzeddine, Al-Mazrou Yagob, *Global Vaccine Action Plan Lessons Learned I: Recommendations for the Next Decade*, Vaccine, Amsterdam, July 2020.

met, and many plateaued, but the increase in coverage has been significant, although this has been affected by the loss of gains as a result of COVID-19. However, climate change will reverse these trends. Even though UNICEF and its partners have been successful in decreasing vaccine prices, UNICEF seeks to go beyond the financial aspects and identify the risks and growth opportunities through further product, production, and corporate-led innovation. Given the carbon emission footprint related to the transport and storage of temperature-sensitive products, such as vaccines, innovations such as controlled-temperature chain, environmentally friendly packaging, as well as the move to regional and local production will become ever more essential. As a global procurement agency, UNICEF has the ability to influence manufacturers' and suppliers' commitment to environmental, social, and governance (ESG) considerations. UNICEF is advocating to industry the need to focus on sustainability, including a growing preference to procure from companies that promote and uphold sustainable production and labour practices (e.g., income equality, diversity, adequate working condition, amongst others), as part of an approach to sustainable procurement and promote local manufacturing.

4.10 Regional manufacturing

The delay many countries experienced in accessing COVID-19 vaccines at an accelerated pace and at scale has resulted in a demand for regionalized vaccine manufacturing, as the pandemic has shown health to be a national security issue. The pandemic also highlighted the benefits countries can have in accessing locally produced health products and the need to encourage increased and expanded regional production and procurement at a regional level, including in Africa. Due attention will need to ensure that such an approach can yield the expected benefits and mitigate the risk of fragmenting markets and undermining gains to be achieved from economies of scale. However, despite exhaustive efforts to ensure countries had equitable access to COVID-19 vaccines, countries with production autonomy were able to prioritize their local needs. Africa is striving to achieve health security by bolstering local production. Both Egypt and South Africa now have the opportunity, through vaccine development, good manufacturing practice (GMP) compliant production and processes, local licensure, and submission of files for WHO prequalification, to offer products that meet international standards for quality, safety, and effectiveness, in response to global tenders from UNICEF and other purchasers. These countries and several others have achieved or are close to achieving the ability and capacity to oversee clinical development, regulate manufacturing facilities, and review and release products. Several African countries have presented their intentions to drive towards African vaccine manufacturing. These countries are at different stages of capacity. In Ghana, the Parliament passed the 2022 National Vaccine Institute Bill in February 2023. The bill proposes establishing the National Vaccine Institute to coordinate and supervise vaccine and serum research, development, and manufacturing.

The African Union (AU) has declared their intent to produce 60 per cent of Africa's vaccines on the continent by 2040. To support the AU, UNICEF is engaging with interested regional manufacturers to provide global market intelligence and information on procurement processes. It also seeks to encourage manufacturers to join its tenders and is signalling the opportunities for regionalization to existing suppliers. UNICEF will also work with Gavi, governments, and donor partners to leverage various mechanisms that will bolster manufacturing on the continent. Relevant examples, such as Uganda, are found through the Partnership for African Vaccine Manufacturing.[70,71] There are heavy investments in Africa by global-level partners and an anticipated 30 potential manufacturers across 14 countries, which will require cautious sustainability considerations.

UNICEF seeks to support the creation of supply security through its long engagement with governments on national immunization programming, from supply chain optimization to equitable access to information on products and capturing demand forecasts, as well as to demand side technical assistance to inform decisions on appropriate national vaccine schedules through national immunization technical advisory groups (NITAGs). With partners, it will also support the information exchange on vaccine markets to inform local or regional manufacturing pipeline decisions. In parallel, UNICEF encourages existing and emerging manufacturers to diversify production in support of building regional capacity, especially for diseases endemic to the region (e.g., Ebola and malaria).

70 Results for Development, *Immunization Financing: a Resource Guide for Advocates, Policymakers, and Program Managers*, R4D, Washington DC, 2017, p 13.
71 United Nations, *Financing for Sustainable Development Report 2022*, The United Nations Inter-Agency Task Force on Financing for Development, New York, April 2022, p. 112.

A demand for vaccines reaching sufficient levels, for example, oral cholera vaccine (OCV) or typhoid conjugate vaccine (TCV) for use in preventive vaccination campaigns, could present a clear case for a regional supply base in Africa. UNICEF continues its efforts with key stakeholders to build capacity and share knowledge and information on public procurement processes and support as an honest broker for African local manufacturing and procurement, including through pooled procurement. Related to this, UNICEF and the Africa CDC have jointly hosted meetings with manufacturers to exchange information to better understand what they see as challenges. UNICEF will continue to work closely with regional partners to empower local governments and manufacturers to build regional suppliers' understanding of markets and procurement strategies. This is occurring in parallel with global partners' support for regulatory harmonization and strengthening.

4.11 The case for immunization financing

Immunization saves an estimated 4.4 million lives a year, helping children survive and thrive, benefiting a wider community. Independent research assessed the impact of these programmes by looking at the vaccination coverage for the ten diseases of HepB, Hib, HPV, Japanese encephalitis, measles, MenA, PVC, rubella, RV, and yellow fever, estimating the mortality and disability-adjusted life-years (DALYs) averted in just under 100 countries between 2000 - 2030.[72]

Research estimates that these vaccination programmes will avert a total of 69 million deaths by 2030, of which 37 million were averted over the past 20 years (2000 - 2019). Most of these deaths were averted amongst children under-five years of age who were immunized against measles. The increase in vaccine coverage and the use of new vaccines has had a major impact on reducing child mortality, which can increase even further with ever-greater immunization coverage. For some pathogens, mortality rates are delayed due to the typically long delay between infection and severe outcomes, notably HepB and HPV. Over the last 20 years, overall mortality declined by 45 per cent against these diseases and by 57 per cent among children under-five years.

The value of vaccines in terms of the investment in immunization against its returns is high and provides value in ways that often go beyond measure when only assessed against child survival and the economic return. Based on a 'cost-of-illness' approach, every $1.00 invested in vaccination delivers a return on investment of $26.35, based on 10 diseases in 24 LICs and MICs between 2011 and 2020. A broader 'value of a statistical life' approach, which captures wider economic benefits, gives an even higher figure for return on investment: around $52.00 for every $1.00 spent on immunization.[73]

However, the world has learned what a loss in sustained engagement implies when it experienced the loss in development gains during the 'lost decade' in the 1980s. During that period, over half of developing countries experienced declining per capita incomes, while developing countries as a group lost 10 per cent of their gross domestic product (GDP) over the whole period. The combined effects defined the period as a 'lost decade', mainly due to the debt crisis that resulted from the massive borrowing by developing countries in the 1970s as a result of the oil price shock of 1973. This was followed by a massive rise in interest rates following the second oil price shock in 1979. Only those countries that were self-sufficient in food and capital goods with negligible foreign debt enjoyed significant economic growth, and which were mainly in Asia. International aid levels did not rebound until 1986 to 1992, when they leapt forward again to reach unprecedented levels, increasing by 12 per cent a year following the collapse of communism and assistance to Eastern Europe in support of economic liberalism.

Developing countries may currently face a similar precipice. The pandemic was responsible for a 6.5 per cent drop in GDP globally in 2020, and IMF projected it to cause a total economic loss worldwide of $28 trillion by 2025.[74] In April 2022, the UN Financing for Sustainable Development Report[75] identified the "great finance divide" as the world starts to experience its worst recession in over 90 years, whereby the poorest segments of societies will be disproportionately affected. The divide is the inability of poorer countries to raise sufficient resources and borrow affordably

72 Li, Xiang PhD, Christinah Mukandavire PhD, Zulma M Cucunubá PhD, et al., *Estimating the Health Impact of Vaccination Against Ten Pathogens in 98 Low-income and Middle-income Countries from 2000 to 2030: A Modelling Study*, The Lancet, Vol 397, Issue 10272, January 2021.
73 UNICEF, *The State of the World's Children 2023: For every child, vaccination*, p.43.
74 International Monetary Fund, *World Economic Outlook, October 2020: A Long and Difficult Ascent*, IMF, Washington, October 2020.
75 United Nations, *Financing for Sustainable Development Report 2022*, The United Nations Inter-Agency Task Force on Financing for Development, New York, April 2022.

to invest in securing the development gains they made over the last 10 years, including those in critical public health services and immunization activities.

Official development assistance (ODA) from official donors in 2021 rose to an all-time high of $178.9 billion as developed countries stepped up to help developing countries cope with COVID-19, and included $6.3 billion spent on providing COVID-19 vaccines to developing countries.[76] However, that still only represents 0.33 per cent of donors' combined gross national income (GNI) and still below the UN target of 0.7 per cent ODA to GNI, a pledge that donor governments initially made at the UN General Assembly in 1970, more than 50 years ago. OECD states are still struggling to reach this level, with the exception of a few northern European states.

Fiscal space, already constrained by the economic impact of COVID-19, is being further exacerbated by the global economic situation, as well as by the impact of the war in Ukraine. However, fiscal equity is critical for equitable and universal social protection. A one percentage point increase in the share of social protection spending going to the poorest quintile is associated with a 0.34 percentage point reduction in poverty headcount at $1.90 a day and with a 0.44 percentage point reduction in the Gini index.[77] Countries spending a higher share of their GDP on social spending, specifically social protection, have lower absolute poverty and inequality. The poverty and inequality reducing impact of the equity measure is as important as the impact of the share of social protection spending in GDP.[78]

The need to achieve vaccine equity has to look

76 The Organisation for Economic Co-operation and Development, *Official Development Assistance (ODA) 2021*, OECD, Paris, 2022.
77 The Gini index, or coefficient, measures the degree of inequality in the distribution of family income in a country.
78 UNICEF, *Strengthening the Evidence on the Correlation Between Fiscal Equity and Social Outcomes for Children*, UNICEF, New York, April 2021.

Mumino Ahmed brought her son Abrahim Mohammed, 4 months old, for vaccination to Gargaar Health Centre in Gambool, Garowe town, Somalia. She lives an hour away in Washington camp for internally displaced people. © UNICEF/Hill

at the pressure on immunization systems. Not just more affordable and accessible vaccines, but the full health system, equally reinforcing cold chain systems, storage capacity, and the need for well-resourced national teams. It needs the strategies able to identify the under-vaccinated and unvaccinated persons, as well as to support coherent planning cycles, with strategic, comprehensive, multi-year and operational annual plans outlining and coordinating strategies and activities. These need an effective monitoring system, with sufficient and adequately appropriated funds to ensure coverage targets, through a modernized vaccine supply chain and management, and an information system that can identify and track each person's vaccination status and vaccination schedules to cover the life cycle course.

Different sections of an immunization programme have different characteristics and different financing needs and implications. Whereas there are different approaches to the procurement of vaccines, whether centrally or regionally, economies of scale can be achieved, and it requires the timely disbursement of funds, as well as to provide suppliers with predictability and can carry long lead delivery times, the actual delivery and the administration of vaccines depends on a shared system also reliant on that of other health services equally dependent on financing.[79]

UNICEF will mitigate this situation by doing more to ensure sustainable immunization financing and offer affordable product options for countries while working closely with governments to support the creation of sustainable domestic financing for health products. With partners, notably Gavi, there is a strong and growing focus on supporting countries to strengthen their immunization financing practices, to ensure budgets cover immunization programming costs. UNICEF will provide financing support to countries via ad hoc pre-financing and bridge financing as well as through the Vaccine Independence Initiative (VII), and through other partners (e.g. the World Bank, the Asian Development Bank, amongst others). The VII, established in 1991, is a financial mechanism that allows governments to bridge temporary budget shortfalls and facilitates the timely procurement of essential supplies. In 2022, the VII facilitated a total of $139.0 million in country pre-financing to accelerate the procurement of vaccines, nutrition and ancillary products. It is a revolving fund that provides countries with pre-financing flexibilities and is made up of recoverable grants to enable investors to retrieve their capital after five years with an interest rate of zero per cent but with the assurance of maximum social impact and leverage. Investors can leave their capital in the fund after investment maturity, transforming their initial investment into a tax-deductible donation in support of UNICEF's work. The VII's scope applies to all essential products beyond vaccines and immunization supplies.

UNICEF established, hosts, and facilitates the vaccine procurement practitioners exchange forum for government-to-government exchange on vaccine procurement-related issues as a framework in UNICEF's efforts to support national governments to strengthen their vaccine procurement practices with evidence-based tools, approaches, and guidelines to support vaccine procurement.

Through its partners, UNICEF has helped significantly increase children's access to vaccines, despite the cost and increasing complexity, and it will keep looking to ensure value for money to the world for children to ensure that they survive and thrive. Immunization is a public health measure that has one of the highest returns on investment, and so UNICEF calls on governments to maintain their investment in immunization to secure the future for the next generations. As we have seen in the pandemic, any gains are not a given, and benefits from immunization strengthen the case for further investment in diversified manufacturing to reach every child. In other words, no one is safe until everyone is safe.

79 Results for Development, *Immunization Financing: a Resource Guide for Advocates, Policymakers, and Program Managers*, R4D, Washington DC, 2017, p 13.

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