U.S. Chamber of Commerce
Global Initiative on Health
and the Economy (GIHE)

Driving Equitable Access to Health Products and Technologies

What is the Role of Localization?

Acknowledgments

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Executive Summary

Key Findings

- Timely, affordable, and equitable access to health products and technologies depends on the interplay of several broad drivers of access.
- Based on an examination of past programs and policies, localization policies alone are unlikely to improve access on a sustained basis. Localization as a tool to improve access only attempts to address the availability of supply and supply-chain issues, leaving many access barriers unaddressed.
- Evidence indicates that the proliferation of localization policies can bring considerable risk to global supply chains and make supply less resilient and less sustainable.
- Regionalization (i.e., expanding and optimizing regional supply chains, including manufacturing capabilities) has the potential to better exploit economies of scale and meaningfully contribute to enabling equitable access. However, regionalization requires the right enabling policies and still needs to be integrated into global supply chains, if it is to avoid the pitfalls identified in this paper.
- Countries seeking to improve equitable access to health products and technologies should look beyond localization and instead consider a comprehensive set of policies and investments that fully address access barriers, secure supply, strengthen healthcare systems, foster regional collaboration, and align resources with policies that work to improve the efficiency and resiliency of the global supply chain for health products and technologies.

This paper sets out to determine what drives equitable access to health products and technologies and examine whether there is evidence that localization (or regionalization) sustainably improves access equity.

Over the last two decades, localization (defined in box) of the production of health products and technologies has been explored as a way to improve equitable patient access. Global inequities in access to COVID-19 health products have intensified these discussions, based on the hypothesis that local production of these products would have improved their availability in low- and middle-income countries. As a result, many stakeholders are promoting localization as a key component of efforts to improve access on a sustained basis and address health security concerns during future crises.

The focus of this research is the relationship between improving equitable access and localization. We recognise that there are other objectives associated to localization policies, particularly industrial and economic development (where there is a substantial literature), but these are beyond the scope of this project.

This paper is intended to be a resource for policymakers and the global health community in designing policy solutions that address access barriers to health products and technologies and ensure better preparedness for future pandemics.

Definitions of key terminologies

Access, localization, and regionalization

- Access: The ease with which individuals and communities can obtain health products and technologies they need.
- Localization: Governments' laws, rules, and measures to build or increase a domestic capacity in a given industry or area of economic activity.
- Regionalization: A form of localization in which parts of the value chain are located in different locations across a region, going beyond the scope of a single country.

Multiple, interconnected drivers across the ecosystem, together, shape access by determining the supply, delivery, and uptake of health products and technologies.

Access to health products and technologies—including therapeutics, vaccines, diagnostics, and medical devices—depends on many drivers. For the purposes of this analysis, these drivers have been organized into 11 broad categories, as shown in the diagram that follows.

The Access Ecosystem

Source: CRA

The access drivers are the healthcare system (infrastructure, funding, and health workforce), the regulatory regime, supply chain management and trade policies, the pricing and reimbursement system, clinical guidelines, awareness and health literacy, legal and IP protections, and industrial policy.

All drivers in the access ecosystem are critical to enabling access—regardless of whether the supply is produced locally, regionally, or globally. Efforts to improve access should examine the drivers individually and as part of the ecosystem. Optimizing access will depend on holistic policies that support these drivers while accounting for their interconnected nature.

Localization alone is unlikely to improve access in a sustainable manner; rather, it can unintentionally be detrimental to access to health products and technologies.

The drivers of the access ecosystem are necessary enablers of access regardless of whether health products and technologies are supplied from local, regional, or global production. Localization and regionalization purportedly seek to improve the supply availability of health products and technologies but leave most access barriers unaddressed.

- In fact, evidence from prior attempts at localization shows that, although intended to improve supply, it can instead undermine supply and hinder access by disrupting critical parts of the access ecosystem, such as the supply chain. For example, further fragmentation of the global supply chain can strain the availability of raw materials and other development and manufacturing inputs.

- Policies that require or force localization can damage access by restricting the international supply of health products and technologies when the ecosystem does not support a viable and sustainable local supply. Many countries lack the necessary human resources and specialized infrastructure to manufacture many health products and technologies.

- Local production of health products and technologies is primarily designed to only address supply availability. However, supply availability itself is only one component of the access ecosystem, and therefore, its impact on patient and consumer access is limited. Further, localization can only address supply availability under very specific circumstances (e.g., when there is sufficient market size to develop economies of scale and sustain demand).

- Localization raises the cost of health products and technologies because it increases the cost of goods (COGs) by decreasing the economies of scale for global supply chains. Local manufacturers often struggle to compete with foreign competitors due to their high prices.

- Localization alone would not have addressed the problem occurring during the COVID-19 pandemic. The supply shortages that occurred during the COVID-19 pandemic were unprecedented because global demand very suddenly exceeded supply. Even when there was supply, many countries lacked the necessary health infrastructure and policy framework to distribute and vaccinate their populations. High-income countries largely adopted an insular approach, driven by health and national security considerations, which resulted in vaccine "hoarding", exacerbating supply shortages in low- and middle-income countries.

- Often, localization policies focus resources on promoting finished goods manufacturing. These are often ultimately unsuccessful (for reasons noted above), resulting in inefficient use of resources and also neglecting opportunities to participate in supply chains for intermediary products.

- Policies that result in investment in non-viable and non-resilient localization efforts could lead to wastage of resources that could instead be used to strengthen the access ecosystem.

Regionalization could be a meaningful contributor to access if supported by an enabling framework.

Relative to country-level localization, regionalization has the advantage of creating a larger potential market, which could allow producers to capitalize on economies of scale and production efficiency. To achieve this, regionalization efforts need to be coupled with supportive policies at both national and regional levels, such as regulatory harmonisation, cross-border trade, advance purchase agreements, and regional supply chain infrastructure and distribution networks. However, maximizing economic efficiency will require supply chains to be global in nature, and end-to-end manufacturing will typically not be possible within a single region.

- Numerous regionalization initiatives have been recently launched, such as the Platform for Harmonized African Health Products Manufacturing (PHAHM), a regional platform to advance the manufacturing of COVID-19 vaccines and other health technologies in the Americas, and the African Vaccine Manufacturing Accelerator (AVMA) amongst others. It is too early to draw lessons directly from these projects; hence, there is a need to use evidence from past examples of localization to the greatest extent possible. Given that regionalization has many, but not all, of the same challenges, we conclude it will not be a silver bullet to addressing the challenges relating to access. Regionalization can only contribute to improving access on a sustained basis if done with a holistic approach.

- Regional manufacturing efforts need to be tied to global efforts to build efficiencies and ensure agility. Integration of all regions into the broader global supply chain as partners is critical for equitable access.

- In terms of pandemic preparedness, regional manufacturing efforts may still be strained during global health emergencies when specific raw materials, such as active pharmaceutical ingredients (API) and manufacturing inputs for medical devices and diagnostics, are in disproportionately high demand. Access to these components via the global supply chain is likely to be the major bottleneck for improving access during these times, regardless of the level of regional manufacturing capacity. In addition, efforts to source regionally, even at a larger scale, may risk undermining wider supply, reducing resilience gained through diversification.

Global health stakeholders are increasingly recognizing the need for regional approach to developing manufacturing capabilities and that this needs to be incorporated in a package of measures. For example, in Africa, we are seeing a shift to regionalization of manufacturing through the Africa Union, the Africa Continental Free Trade Agreement, in addition to the initiatives described above. These reflects the recognition that regional trade zones are needed to improve market size, alongside foundational elements such as regulatory harmonization; only through a holistic approach will access to health products and technologies improve.

Policymakers and the global health community should focus on introducing a supportive package of policies and initiatives that target the whole access ecosystem—addressing access barriers, securing supply, and strengthening healthcare systems.

Policies to achieve this at the national level should include, but not be limited to, the following:

- Implementing efficient regulatory mechanisms by adopting regulatory reliance and recognition, digitalization of regulatory processes, and regulatory convergence to international best practices and standards.

- Addressing trade barriers and supply chain bottlenecks through measures to ensure the free flow of products across borders and efforts to improve infrastructure and facilities for receiving, storing, distributing, and administering different types of health technologies.

- Optimizing healthcare funding, infrastructure, and workforce by increasing national health budgets and introducing efficiencies in spending to improve health service delivery for patients and reduce out-of-pocket (OOP) payments.

- Leveraging value-based procurement criteria that consider not only price but also quality, supply resilience, competition, and value to patients, healthcare systems, and society.

- Strengthening intellectual property (IP) protection mechanisms to international standards to increase access to innovative health technologies.

- Improving demand forecasting and generation through the development and regular update of clinical guidelines and the use of health information systems.

- Improving awareness and health literacy of the population to facilitate uptake of available health products and technologies.

Supportive policies also need to be implemented regionally to foster regional collaboration, including but not limited to the following:

- Regulatory convergence: Regional harmonization of regulatory requirements that adhere to international standards and best practices, reducing unnecessary, redundant reviews and the burden on regulatory authorities.

- Purchase agreements and minimizing trade barriers: Governments in a region can improve the viability of a sustainable regional market by reducing regional trade barriers and creating an open market (discouraging forced localization policies that hinder trade). Furthermore, governments and other procurers need to commit to supporting market formation within a region through advance purchase agreements.

- Supply chain optimization: Strengthened regional supply chain infrastructure, processes, distribution networks, and facilities to ensure countries can receive, store, distribute, and safely administer health products and technologies. In addition, there is a need to strengthen the resiliency of the upstream supply chain of APIs and other raw materials to ensure supply security, particularly during health emergencies.

- Fostering new collaborations: There is a shared desire to improve equitable access. Manufacturers who export globally have a unique perspective on how to improve supply sustainability and to achieve the objectives articulated by policymakers. Their role in the exceedingly complex global supply chain (with individual companies working together at unique points in the value chain and across many countries) makes engagement and knowledge sharing critical to ensure sustainability. Policymakers need to foster new collaboration across global health actors in the public and private sectors to ensure investments and policies are aligned with sustainable access and avoid unintended consequences.

By introducing the above policies to address access barriers, policymakers can simultaneously improve equity, pave the way for a sustainable local health technology industry, and attract further investment from global manufacturers.

Introduction

The Global Initiative on Health and the Economy at the United States Chamber of Commerce commissioned Charles River Associates (CRA) to develop an analysis of the barriers to equitable access to health products and technologies (therapeutics, vaccines, diagnostics, and medical devices) and whether localization could play a role in enabling access.

The debate on the role of localization in improving access is not new.

Improving access to health products and technologies has long been a priority issue for the global health community, but in the last two decades, increased attention has been paid to whether local production could foster access to these products and technologies.[1,2] Advocates of localization consider it a mechanism for improving resilience in the supply chain and maintaining local supply. They hope that localization of manufacturing of goods can improve domestic access to health products and technologies. However, the available evidence suggests localization alone is unlikely to deliver these outcomes.

The focus on localization as a policy tool to improve access has intensified since the COVID-19 pandemic.

During the COVID-19 pandemic, there were significant differences in how quickly countries could gain access to vital health products and technologies, most notably vaccines. High-income countries largely adopted an insular approach, driven by health and national security considerations, which resulted in vaccine "hoarding".

This led to the hypothesis that the availability of these technologies, particularly in low- and middle-income countries (LMICs), would have been greater had local production been in place and that local manufacturing capabilities are needed to ensure access to health products and technologies, including, but not limited to, during any future pandemics. As a result, many stakeholders are promoting localization as a key component of efforts to improve access on a sustained basis and address health security concerns during future crises. While advocacy for localization has been particularly pronounced in LMICs, it is being discussed globally.[3]

For example, since the pandemic, there have been discussions on reshoring and localizing the production of API as an approach to secure the supply in the European Union (EU).[4] In France, recent public procurement policy includes local production as an award criterion for hospital tenders with the aim of addressing the security of supply issues in upcoming tenders.[5] Under this policy regime, suppliers of certain products (specific molecules) must ensure that raw materials originate from a Member State of the EU and that the supplies procured through the contract are manufactured entirely or in part by production branches within the EU territory.[6]

A series of reports have examined localization policies (defined in Box 1) as a tool of industrial policy and economic development.[7,8] This is not the aim of this paper, which instead looks at the relationship between localization and access in the same jurisdiction, which has received little attention to date.

Box 1: Definitions of key terminologies

Access, localization, and regionalization

- Access: The ease with which individuals and communities can obtain health products and technologies they need.[9]
- Localization: Governments' laws, rules, and measures to build or increase a domestic capacity in a given industry or area of economic activity.[7]
- Regionalization: A form of localization in which parts of the value chain are located in different locations across a region, going beyond the scope of a single country.

It is essential to distinguish between different types of localization:

- Incentivized vs Forced: Some countries have sought to achieve the objectives of localization primarily through positive, non-discriminatory incentives for investment. Other countries have taken a different approach by establishing requirements (such as local content requirements) for various degrees of local investment from foreign manufacturers seeking to access the local market—this is often referred to as forced localization.[7]
- Localization vs Regionalization: There are policy proposals that focus on encouraging activities across a geographic region (regionalization) rather than in individual countries. We focus primarily on national policies but also discuss how the debate is increasingly considering regionalization.

This white paper first examines the factors affecting access to health products and technologies and then examines whether localization could improve access.

Our intention is for this paper to be a resource for policymakers and the global health community in designing policy solutions that address access barriers to health products and technologies and ensure better preparedness for future pandemics.

Methodology

We developed the white paper in three stages. The first stage was to conduct a structured literature review to identify access barriers to different types of health products and technologies in pandemic and non-pandemic contexts. The literature review included the academic literature, government reports, non-government agency studies, and gray literature.

The second stage was to examine the evidence that previous localization policies had an impact on access. We did this by developing a series of country case studies. The case studies included countries from different regions and income levels.

They were chosen because they had implemented localization policies in the last two decades (so it was possible to observe what had subsequently happened). Although most of the case study countries are LMICs, we included evidence from high-income countries (HICs) in recognition that localization policies are being debated globally and in countries of all income levels. Selected countries were as follows (Figure 1):

- Africa: Algeria and South Africa
- Asia: India, Indonesia, and Singapore
- Latin America: Brazil

Figure 1: Case study countries

Source: CRA

The last stage was interviews involving six notable organizations in the global health community (the Bill and Melinda Gates Foundation, the Federation of African Pharmaceutical Manufacturers Associations, Inter-American Development Bank, the Lawrence J. Ellison Institute for Transformative Medicine, Unitaid, USAID, and WHO) and five industry representatives from the biopharmaceutical, diagnostics, and medical device sub-sectors. The interview program had three objectives. The first was to elicit stakeholder insights, including global health community perspectives on critical elements for improving access and the role of localization. The second objective of the interview program was to validate insights generated from the literature review and case study analysis. The third was to gather views on potential policy recommendations for improving access.

In terms of scope, the focus of this research is the relationship between improving access and localization.

- Issues around industrial policy and economic development are referenced, but the scope of our research does not address those goals of localization policy.
- The focus is on examples where we could observe the impact of the policy's introduction. Many of the current policies focusing on regionalization are still under discussion or only recently introduced. It is too early to draw lessons directly from these projects; hence, there is a need to use evidence from past examples of localization to the greatest extent possible.
- To better understand the specific impact of localization, we excluded examples of localization that were introduced alongside policies facilitating compulsory licencing (such as local production of direct-acting antivirals for hepatitis C infection).
- Furthermore, we acknowledge that 'health product' is a broad term, and there are other examples of localization that exist for simpler-to-manufacture health commodities, including personal protective equipment and bed nets, where the lessons may differ. The literature review did not include these types of products. We focused on vaccines, therapeutics, medical devices, and complex diagnostics.

Drivers of equitable access to health products and technologies

Lack of access to health products and technologies has long been a priority issue for the global health community. Despite this, as many as two billion people lack access to essential health products and technologies—therapeutics, vaccines, medical devices, and diagnostics.[10] In this chapter, we outline our findings on the key barriers that prevent access to health products and technologies, drawing on interviews with global health stakeholders and the available literature.[11,12]

The access ecosystem is composed of multiple interacting drivers.

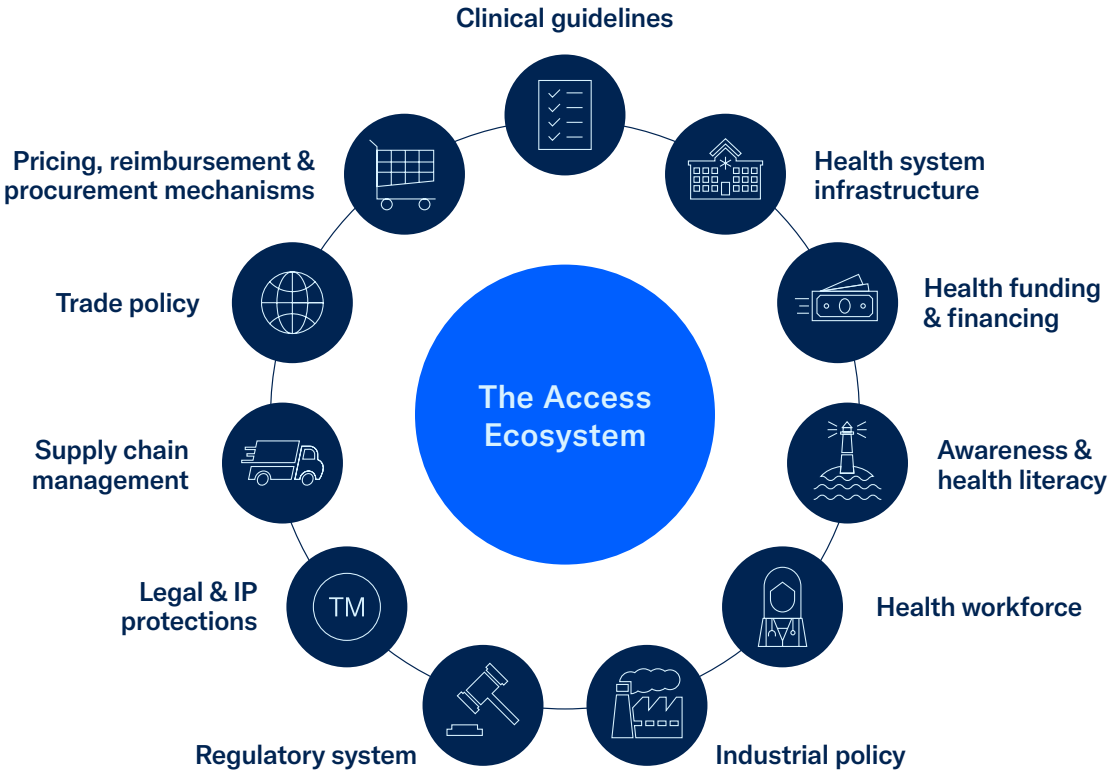
It is essential to consider the drivers of access as an ecosystem. Access to health products and technologies is a function of multiple drivers interacting to facilitate the supply, delivery, and uptake of health products and technologies. We identified 11 broad drivers associated with the healthcare system (infrastructure and funding, health workforce), the regulatory and IP regime, supply and trade policy, industrial policy, pricing and reimbursement system, availability of clinical guidelines, and awareness and health literacy. The interplay of these components creates the access ecosystem (Figure 2). Policies relating to these drivers must be optimized to facilitate equitable and sustainable access to health products and technologies.

These drivers apply to all countries independent of income, but some are more often a challenge in LMICs,[13–15] while others are more commonly associated with barriers in higher-income countries. The broad consensus among global health stakeholders interviewed was that some drivers require more immediate attention to optimize the access ecosystem and address key access barriers in LMICs. These include strengthening the regulatory system, improving supply chain infrastructure and processes, fostering policies to reduce trade barriers, and optimizing healthcare funding, infrastructure, and workforce.[16] In higher-income countries, attention is often needed to address barriers in pricing, reimbursement, and procurement mechanisms.[17–20]

Regulatory hurdles constitute a significant barrier to access in LMICs.

Regulatory systems entail the processes and legal frameworks governing clinical trials, manufacturing, marketing approval, and monitoring ongoing safety and effectiveness. These are vital for ensuring safe, efficacious, and effective health products and technologies.[21] Regardless of whether production is located globally, regionally, or locally, regulatory systems are crucial for ensuring access to medicines, preventing counterfeit or substandard health products and technologies, attracting investment, and boosting patient confidence and safety.[22,23]

Figure 2: The Access Ecosystem



Source: CRA analysis

Regulatory systems play a critical role in the cross-border supply of health products and technologies. To manufacture goods in one country and export to another, the importing country must accept regulatory approval and standards from the exporting country or have a competent agency and regulatory process that facilitates trade.

Following the evaluation of a health product or technology, marketing authorization (MA) or approval is usually the entry point into healthcare systems. The process of granting MA could constitute a barrier to access if unnecessarily restricted due to issues with regulatory capacity or processes.

Weaknesses in the regulatory environment constitute a barrier to access. These include but are not limited to:

- Regulatory duplication and lack of consistency: Multiple regulatory systems worldwide mean many different submission requirements and standards (sometimes diverging from international standards), creating duplication and delay that increases the burden on manufacturers when seeking regulatory approval and hinders patient access.[21,24,25] In many countries, particularly LMICs, regulatory processes are not often streamlined to ensure harmonization and compliance with technical standards across countries and minimize duplication of dossier reviews.[21,24,25]

- Rigid regulatory process: The use of electronic regulatory processes such as electronic submissions and signatures, as well as digitalization of other regulatory processes, has been found to be useful

during both normative processes and health emergencies and can help facilitate timely access to health products and technologies. The lack of regulatory agility in many LMICs further delays the availability of safe and effective health products and technologies, and in particular during a public health emergency.[26–28]

- Delays in regulatory approval timelines: Often arising due to limited financial resources, limited personnel capacity, and inefficient regulatory processes, regulatory delays are frequently cited as a barrier to access. There are delays in approving new health products across countries of all income levels, with LMICs typically facing greater delays. Approval time could be well over 1,000 calendar days in sub-Saharan Africa, 400–500 calendar days in Asia (India, Taiwan, Singapore, South Korea, and Malaysia), and around 400 calendar days in Latin America.[29–35] Among HICs, median approval times in Canada, the EU, and the United States (US) were 364 days (343–651), 371 days (322–434), and 304 days (209–455), respectively.[36,37]

- The prevalence of substandard and falsified products. It has been reported that as many as one in ten medical products in LMICs are substandard or falsified.[38] In addition to reducing patient and physician confidence, this directly reduces access to effective treatment. This has been linked to weaknesses in the regulatory systems in LMICs and affects both locally made and imported products.

Some improvements have been noted over the last ten years, as the National Regulatory Authorities (NRAs) in many LMICs have attained the WHO maturity level 3 (ML3) for health products (medicines and vaccines), which represents the minimum maturity target for NRAs.[39] However, further improvements addressing remaining regulatory weaknesses would be valuable, particularly for medical devices and in vitro diagnostics (IVDs).

Trade barriers can prevent access.

No single country can be entirely self-reliant in producing health products and technologies for medical care or the necessary intermediate products. Even with local production, no product is wholly made within a single country. Most countries rely heavily on imports of intermediary or finished products obtained via the global health supply chain.[40]

Trade barriers such as tariffs on imported health products and technologies often lead to higher prices, thereby undermining access.[41] This can be particularly challenging for products with complex manufacturing processes involving activities in many countries and complicated supply chains. Medical devices are often used as a case study to illustrate this.

Trade barriers can also take the form of export restrictions, which exacerbated access challenges during the pandemic. A number of countries imposed temporary restrictions on exports of certain medical goods, including vaccines (vaccine hoarding) and personal protective equipment. This prompted calls for more geographical diversification of the manufacturing of medical goods.[42,43] The negative impact of these export restrictions on the global trading system and pandemic response is well documented.[42,44,45] Furthermore, there were concerns that this would jeopardize integrated global supply chains.[42,44] Interviewees were concerned about the role of trade barriers in limiting access to COVID-19 vaccines and other health products and technologies during the pandemic.

Some access barriers specifically relate to trade barriers:

- Many countries continue to impose duties on health products and technologies, which not only drive up the prices but also limit their availability.[46]

- Trade restrictions limit access to health products and technologies that cannot be locally produced.

Again, there have been improvements as countries have invested in supply infrastructure. There have also been regional efforts to reduce trade barriers, such as the Africa Continental Free Trade Agreement (AfCFTA), which aims to create functional economic integration with easy flow of goods and services between countries on the continent. This is an example of a positive plan to address cross-country investment opportunities, remove trade barriers, and address this barrier of access.

Supply chain bottlenecks undermine access.

The efficiency and resilience of the supply chain of health products and technologies, from manufacturers to patients, is a key driver of access. The production of health products and technologies involves individual companies, often located in different countries and regions, who specialize in specific steps of the production process. This involves raw materials and intermediary products sourced from different geographical origins.[40] Disruption to global supply chains and production networks can directly impact the manufacture and supply of intermediary and finished products and reduce access.

Weaknesses in downstream supply chain infrastructure and processes, including cold chain requirements, warehousing/storage, distribution, and procurement, can introduce additional barriers. There has been particular interest in their impact on access to vaccines and highly innovative therapeutics such as biologics.[47] The nature of these products makes the supply chain complex, necessitating resilient management to ensure access.[48]

There are many access barriers relating to downstream supply chains that prevent access to health products and technologies:

- In many countries, there are weaknesses in the supply chain processes of health products and technologies, resulting in frequent stockouts,[49] Some root causes of stockouts at health service delivery points include low commitment to funding operating costs, lack of supply chain planning data for demand forecasting, weak planning capacity, and lack of incentives to improve supply chain performance.[50] All of these contribute to supply instability downstream.

- There are also weaknesses in supply chain infrastructure affecting particular types of products, especially lack of investment in cold chain facilities. For example, many vaccines require cold chain infrastructure and modern technology from the time of manufacture until the point of administration if they are to be safe and effective.[51]

- Procurement policies are often not value-based and consider only price but not quality of products or ability to supply, and do not take into account supply resilience.[52,53] Numerous reports suggest that the adoption of multi-criteria procurement evaluations is key for fostering sustainable long-term supply. However, implementation of these practices has been slow. Procurement processes often do not include a guarantee of volumes or multi-year demand visibility to enable manufacturers and suppliers to plan accordingly and offer more competitive proposals during the procurement process.[54] Additionally, procurement mechanisms that lead to single-winner awards undermine the security of supply.Many stakeholder groups (including suppliers, procurers, and authorities) agree that multi-award contracts contribute to the security of supply.[5]

Limited funding and investment in health infrastructure, including the capacity of the health workforce, are key barriers to the delivery and uptake of health products and technologies.

Once health products and technologies have navigated the regulatory and trade processes and are commercially available, patient access depends largely on the healthcare system. Sufficient funding is a critical factor determining the uptake of health products and technologies. This includes funding for health system infrastructure, workforce, and procurement of health products and technologies, as well as financing for healthcare access to ensure out-of-pocket (OOP) spending on healthcare is minimal and affordable for patients. The share of revenues from OOP spending as a proportion of current health expenditure (CHE) indicates how much is funded directly by households' OOP expenditure on health. OOP spending, as a proportion of CHE, greater than 40 percent is generally considered high.[55] High OOP spending is associated with catastrophic and impoverishing household spending and is regarded as a major access barrier.[56] In settings with limited health insurance coverage, the burden of healthcare expenses borne by individual patients and households is significant and negatively impacts access to health products and technologies.[57]

The delivery of health products and technologies depends on physical infrastructure, such as hospitals and clinics, and the expertise of the health workforce (including clinicians, nurses, diagnostic specialists, and pharmacists). The availability, accessibility, and administration of health products and technologies have been strongly linked to investment in the number and distribution of healthcare workers per capita in any setting.[58,59]

In addition to adequate workforce and infrastructure, there needs to be information and awareness of the value that health products and technologies deliver. The lack of clinical guidelines also limits the uptake of health products and technologies.[60]

Access to health products and technologies often also requires that patients seek healthcare. This depends on health awareness and general health education but also affordability. Lack of awareness, stigma, and poor health literacy of the population negatively influence health-seeking behavior and make demand generation and uptake of health products and technologies challenging.[61–63]

Given the current healthcare funding levels globally, the following areas have been identified as constituting access barriers.

- Limited investment in healthcare infrastructure for delivering health products and technologies to patients contributes to geographical health inequity.[64,65]

- Many countries currently have a significant shortage of healthcare workers and this has a negative impact on the utilization of health services and uptake of health products and technologies.[58,66,67]

- High OOP spending on healthcare is prevalent in LMICs and continues to be a problem in countries with higher income levels.[56,68] In many countries in Africa, OOP spending as a proportion of CHE exceeds 40 percent. In countries such as Cameroon, Equatorial Guinea, and Nigeria, it is more than 70 percent.[69,70] In LMICs in Asia-Pacific, the proportion of OOP spending is about 40 percent on average and well over 60 percent in some countries.[71] In Latin America and the Caribbean, it is 34 percent, much higher than the OECD average of 21 percent.[72] The high prevalence

of OOP payments, combined with the relatively lower wages in LMICs, exacerbates the risk that patients will not procure life-saving health products.[15,73]

Some progress has been made in increasing the number and quality of healthcare workers globally, and a recent analysis to 2030 shows a projected health workforce growth rate of nearly 3 percent annually (compared with less than 1 percent growth of the global population). However, this global progress is uneven, and much needs to be done to ensure equitable progress across regions.[74]

While it is encouraging to see governments around the world in 2023 recommit to scaling up efforts to reverse the trend of rising OOP health expenditures by 2030,[60] this commitment needs urgently to become a concrete investment that would reduce the proportion of OOP spending globally, particularly in LMICs.

Pricing and reimbursement policies can create an unsustainable market, leading to supplier consolidation and supply disruptions.

Pricing and reimbursement policies vary significantly from country to country and between types of health technology. There are concerns the current pricing and reimbursement systems are unsustainable and pose access barriers.[75] These systems often prioritize the lowest-cost options, neglecting quality, long-term health outcomes, and the necessity of investing in sustainable supply chains and manufacturing practices. This emphasis on cost minimization and austere pricing policies (to the exclusion of other considerations) can lead to market consolidation and increased vulnerability to supply disruptions.[76] Further, the inability of manufacturers to adjust prices to accommodate inflation in production costs can make certain products economically unviable, and they risk being withdrawn from the market.

There is a need for the implementation of more sustainable value-based pricing models to balance competing objectives. By restructuring these systems to better recognize and reward investments in robust manufacturing and supply processes, policymakers can help mitigate the risks of shortages and ensure more reliable access. Such reforms are crucial for maintaining the integrity of healthcare systems and the continuous availability of essential health products and technologies.

Improving access ultimately depends on addressing barriers across the entire ecosystem.

There are immediate priorities for LMICs and HICs to reduce barriers to health technologies, but optimizing all the drivers affecting the access ecosystem is necessary for ensuring equitable access to health products and technologies in all countries.

- All drivers in the access ecosystem are critical to enabling access—regardless of whether the supply is produced locally, regionally, or globally.

- Efforts to improve access should examine linkages between the drivers and see them as part of the ecosystem. Optimizing access will depend on holistic policies that support all access drivers while accounting for their interconnected nature.

Annexes 2 and 3 provide additional details on each driver of access identified through the literature review and interview program.

The impact of localization policies on access

To understand if localization plays a role in improving access, we first consider the policy motivation for localization and the recent policy debate. We then consider the evidence that localization policies can have an impact on access (by examining six case studies—five LMICs and one HIC—as set out in Table 1). To observe the impact of localization, we have chosen countries in which localization was introduced some time ago.

Globally, there is increased interest in using localization to improve access.

The COVID-19 pandemic led to a significant shift in attitudes towards localized manufacturing. In the emergency context of the pandemic, local production was seen as a way of guaranteeing access and health security. While COVID-19 is no longer an international public health emergency, the localization debates that it prompted have continued. Some of the notable initiatives include:

- World Local Production Forum: This global platform for discussions on strengthening local production was launched in 2021.[1]
- Platform for Harmonized African Health Products Manufacturing (PHAHM), formerly Partnerships for African Vaccine Manufacturing (PAVM): This regional platform aims to fulfill the African Union's continental vision of producing 60 percent of vaccines, therapeutics, and other medical products by 2040.[77]

Table 1: Year of introduction of localization policy across case study countries

Algeria (DZA)	Brazil (BRA)
2008	2012
India (IND)	**Indonesia (IDN)**
~1980s	2008
Singapore (SGP)	**South Africa (ZAF)**
2000	2003

- African Vaccine Manufacturing Accelerator (AVMA): In collaboration between Gavi, the Africa Union, and the Africa Centres for Disease Control and Prevention (Africa CDC), the AMVA initiative was established as a financing mechanism to make up to US$1 billion available over ten years starting from June 2024 to accelerate the expansion of commercially viable vaccine manufacturing in Africa.[78]

Figure 3: Examples of policies targeted at localization along the value chain

Example of localization policies	Policies and investments along the value chain that force or incentivize localization			
	R&D/manufacturing	**Regulatory approval**	**Trade and supply**	**Commercialization**
	Technology transfers and product development partnerships R&D tax credits Investments in training a skilled workforce and developing strong clinical trial networks Strong IP regime	Expedited approval for locally manufactured products	Import bans if local manufactureres exist	Pricing and reimbursement advantages for locally manufactured products
		Local manufacturing requirements for approval	Incentives for domestic manufacturing e.g., tax incentives Removal of trade barriers	Preferential treatment in tenders and procurement for products manufactured by local of national companies

Source: CRA analysis

- Regional platform to advance the manufacturing of COVID-19 vaccines and other health technologies in the Americas: This collaborative regional platform was launched in 2021 by the Pan American Health Organization (PAHO).[79]

- Initiative for reshoring API production: In the EU, ongoing policy discussions aim to localize API production within the EU territory.[4]

These recent initiatives have been announced in the wake of the COVID-19 pandemic, so it is not yet possible to assess their impact on local production and access that is hoped to follow. Instead, to understand the role of localization, we need to look at policies that have been in place for a longer period, using the case studies above. These illustrate policies affecting one or more components along the value chain for health products and technologies, as shown in Figure 3.

These policies can be directed at research and development activities, manufacturing, commercialization phases, and the delivery of health products and technologies to patients.

To understand localization, we need to consider its objective - where localization focuses on access; it is mainly designed to address domestic supply availability.

Localization policies—insofar as they aim to improve access rather than other objectives, such as supporting the local industry—mainly seek, by design, to improve the domestic availability of health products and technologies.

Where localization focuses on supporting local industry, it is only successful when it is incentivized and not forced.

Sometimes, localization objectives are pursued with the primary aim of developing local industry. Countries have sought to achieve this objective using two main approaches—forced localization or incentivized localization measures, or a combination of the two. However, evidence suggests that countries,

Box 2: Key investment areas in developing a sustainable export-driven manufacturing ecosystem in Singapore

Singapore

Singapore has a long history of supporting the localization of different parts of the industry value chain. In 2000, Singapore launched its biomedical strategy aimed at transitioning the country to a world-class location for biomedical activities across the whole innovation and manufacturing value chain. The key features of this transition include a set of objectives with corresponding policy actions:

- Acquiring world-class scientists and talents
- Developing a large stock of human capital in biomedicine
- Developing an enabling research infrastructure and environment
- Raising venture capital through public-private partnerships
- Providing tax incentives
- Implementing a strong regulatory framework and IP protection mechanisms.

By adopting this long-term strategic approach, rather than simply requiring local manufacturing, Singapore's biopharmaceutical sector grew significantly in less than two decades. As of 2019, the biomedical manufacturing sector represented 20 percent of total manufacturing value added (S$19.57 billion) and 4 percent of Singapore's gross domestic product (GDP). The number of manufacturing sites for biological drugs grew from 0 to 18.[8] In fact, Singapore is now one of the few countries with a positive pharmaceutical trade balance: its exports of manufactured pharmaceuticals are more than twice the value of its imports.[80] The success of Singapore's local manufacturing is in part due to its export-driven strategy.[16]

In the same period, access to health products and technologies has also improved, although this is not necessarily related to the increased capacity for local production of medical goods but more attributable to the various healthcare policies implemented by the government, such as the national insurance schemes and subsidies to increase the availability and affordability of healthcare.[81]

Notably, despite its increased local production capacity, Singapore still relies on imports for many health products and technologies.

such as Singapore, that have sought localization mainly by implementing positive, non-discriminatory incentive-based policies have been more successful in developing their local industry.[7] Such policies aim to attract foreign investment in the country by providing a package of incentives such as tax benefits and an industrial policy that fosters a conducive environment for sustainable manufacturing and export, including modern infrastructure, a robust regulatory framework, and a strong IP regime (Box 2).

Developing local industry through localization, even when incentivized, does not necessarily improve access. To improve access, there need to be deliberate policies focusing on the access ecosystem.

Box 3: Case study highlighting the importance of market size and market predictability (South Africa)

South Africa

Through various localization initiatives, the South African government has been actively fostering the growth of local manufacturer vaccine Biovac, enhancing its capabilities and capacity for vaccine production. Collaborative technology transfer agreements were established with Pfizer and Sanofi, enabling Biovac to establish the continent's largest state-of-the-art cold chain facility. This partnership not only bolstered the security of vaccine supply for the Extended Programme on Immunization (EPI) but also facilitated skills development, capability building, and job creation within the South African economy. Initially employing over 30 individuals, Biovac's workforce expanded to more than 500 by the end of 2022.

However, despite these advancements, Biovac has faced challenges due to the limited domestic market size in South Africa and regulatory hurdles in exporting to other markets, hindering its ability to achieve the economies of scale necessary for cost competitiveness with international manufacturers. For example, Biovac's COVID-19 vaccine is not yet included in WHO Emergency Use Listing,[82] therefore, before this product can be marketed in other countries, it will require full registration in these countries, which could take years. As the South African Health Products Regulatory Authority (SAHPRA) is not yet at the highest maturity level (ML 4) in the WHO classification of regulatory authorities for medical products,[39] other countries may not rely on the evaluation done by SAHPRA but carry out their own independent evaluation.[54] This regulatory hurdle undermines Biovac's ability to export to other countries and achieve economies of scale.

In addition, Biovac lost a government tender for its pediatric pneumonia vaccine to an Indian-backed manufacturer offering cheaper pricing of a lower valent vaccine option.[83] Despite substantial investments and governmental support, Biovac has struggled to establish a sustainable operating model due to incongruent policies and other prevailing healthcare challenges, even with the availability of supply.

In practice, localization alone is unlikely to address the domestic availability of supply.

Even if the goal is to improve supply availability, localization policies in practice often do not improve domestic supply. As with many high-tech production processes and supply chains, they are dependent on economies of scale, factors affecting efficiencies in production, predictable and stable volume forecasts and demand, and prices that recognize value and affordability. As such, without the right market conditions, localization alone is unlikely to increase domestic supply (Box 3).

The South African case study is consistent with the wider literature, which finds that country-level localization focused on a relatively small domestic market size without an export-driven strategy, congruent policy environment, and a supportive ecosystem to sustain manufacturing has been unsuccessful.[8] These examples illustrate the risk that localization raises the cost of health products and technologies because of higher COGs resulting from the loss in economies of scale. This means local manufacturers will struggle to compete with foreign competitors, who can exploit economies scale.

Box 4: Case study highlighting the importance global supply chain and the role of local and export markets (India)

India

The large consumer market and export-driven manufacturing have played a critical role in the success of local production of health products (particularly vaccines and generic medicines) in India.[84,85] The large local demand for childhood vaccines (25 million newborns each year) through the government-sponsored Universal Immunization Program[86] and the high demand for low-priced vaccines by UNICEF and Gavi for their global immunization programs have contributed to India's success in vaccine production.[87] These have provided local manufacturers with a large, reliable local and export market to invest in, developing volumes sufficient to benefit from economies of scale.

However, the same is not true for medical devices and in-vitro diagnostics, in which local manufacturers face challenges exporting their products due to differences in regulatory requirements and standards, as India has yet to converge to international best regulatory practices and standards for these types of technologies.[54] India has yet to become a full member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.

It is important to recognize that production in India is part of the global supply chain. For medicines, as with many other countries with significant generic production, India is also dependent on China for upstream chemical inputs.[88]

There are also lessons regarding procurement policies. These should focus on sustainability and the provider offering the best value proposition. Procurement organized to favor a particular bidder is not sustainable over time. Equally, it is also harmful if procurement mechanisms (such as tenders) are only based on the lowest price, undermining market predictability. Instead, value-based procurement mechanisms offer the best alternative to improving access on a sustainable basis.

There are very few countries or regional trade zones that have sufficient market size and a complement of foundational elements to sustain manufacturing and the development of local production of health products and technologies. While India does not have the innovation ecosystem to develop new health technologies, it is an interesting example from a manufacturing viewpoint (Box 4).

Box 5: Barriers to regionalization in Africa

South Africa

Aspen Pharmaceuticals (Aspen) secured technology transfers that enabled them to fill and finish Johnson & Johnson's COVID-19 vaccines, with the aim of supplying vaccines regionally. However, Aspen ultimately did not receive any orders from African countries for a number of reasons.[89] One of the reasons was due to the time it takes to ramp up production – by the time there was effective production, there was widespread availability of vaccine supplies from alternative sources – as a result, Aspen's expected orders for Johnson & Johnson COVID-19 vaccines from African nations did not materialize. Furthermore, given the need to administer these vaccines promptly before expiry countries were cautious about acquiring more doses, fearing surplus accumulation and potential wastage.

As a result, Aspen ceased production at a point when 84 percent of the African population remained unvaccinated. Further demonstrating that localization cannot improve access, improving the regional supply of the COVID-19 vaccine was ineffective in improving access and vaccination rates.[89]

More recently, the debate around localization has shifted towards regionalization. Theoretically, regionalization could solve the market size issue by aggregating demand across countries rather than segmenting it within a country's borders.

Although supported by some stakeholders, fragmentation between countries in many regions currently appears to make regionalization impracticable. Recent regionalization efforts have yet to put in place the supportive measures at both national and regional levels that would be necessary for successful regional collaboration, including regulatory harmonization, policies to enable cross-border trade and regional supply chain infrastructure and distribution networks; additionally, governments and the other procurers need to commit to supporting market formation within the region through advance purchase agreements (Box 5).

Ultimately, regionalization is a variation of localization and is likely to suffer from many of the same pitfalls if not supported by a set of enabling policies that create the right market conditions and allow integration into global supply chains. For example, Moderna, in response to calls from African governments and global health stakeholders during the pandemic to localize the manufacturing of vaccines in the region, planned to build an mRNA vaccine manufacturing facility in Africa to produce COVID-19 vaccines and other vaccines. However, the company recently announced its decision to pause building the vaccine manufacturing facility while it determines future demand for mRNA vaccines on the African continent. Since the pandemic, demand for COVID-19 vaccines has declined and is not sufficient to support the viability of local manufacturing. The company noted that it had not received any vaccine orders for Africa since 2022 and faced the cancellation of previous orders, resulting in more than $1 billion in losses and write-downs.[90] This development further demonstrates that localization or regionalization alone is unlikely to succeed without the right market conditions.

Box 6: Case study highlighting how forced localization undermines the availability of health products

Indonesia

In 2008, the Indonesian Ministry of Health implemented forced localization policies (Decree 1010/ MENKES/PER/ XI/2008) that prevent companies from gaining marketing authorization unless registered as a local pharmaceutical industry participant.[8] This decree requires companies to set up local manufacturing plants or partner with existing local manufacturers in order to receive market authorization. Under Decree 1799/2010, the manufacturing requirement was slightly relaxed to allow domestic labeling and packaging activities to qualify as local production. This policy sits alongside various other attempts to boost local industry, such as requiring local product prioritization over imports in government tenders. While there has been some growth in local manufacturing with an increase in the share of local industry since the implementation of the localization policies,[91,92] these policies have not addressed many access challenges in the country. It has been reported that the restrictions imposed by the legislation resulted in significant delays in access to or unavailability of medicines, particularly for internationally produced medicines.[91]

In 2014, the government of Indonesia launched a nationwide universal health coverage (UHC) scheme (JKN scheme) to improve access to healthcare. At the start of 2023, the scheme had registered more than 253 million participants, representing 93 percent of the population.[93]

Based on available evidence, the availability of essential medicines appears to be higher in the period when the UHC scheme was being implemented than when only localization policies were in place. A study assessing the availability of medicines in Indonesia in 2014 revealed that only 50 percent of the drugs on the WHO-recommended Essential Drug List (EDL) were available in the local market.[7] A recent study in 2024 found that, under the JKN scheme, 72 percent of essential medicines were available. The study further noted that the median availability of 17 priority medicines was 82 percent, which is relatively high compared to other countries in the region.[93] Access policies, such as the JKN scheme, appear to improve the availability of essential medicines in Indonesia more than the localization policies.

The need for a more holistic approach has been recognized in some initiatives. For example, the PHAHM initiative in Africa was recently launched, and although it is too early to assess its impact, it appears to be taking a holistic approach by focusing on creating a sustainable access ecosystem that can enable the right market conditions. Judging by its framework for action, this regional initiative acknowledges that localization by itself does not guarantee access.[77]

Policies forcing localization can limit supply availability.

Forced localization policies, such as local content requirements, have the potential to be particularly damaging by making it difficult for international manufacturers to achieve market access (Box 6). This can severely damage patient access to many health products and technologies that a given country does not have the capacity to develop and efficiently produce locally.[8] Evidence suggests that forcing localization does not necessarily increase access to either essential or innovative health products.[7]

Localization policies can have unintended consequences, damaging equitable access to health products and technologies.

There is evidence to suggest that localization policies could hinder access by disrupting key parts of the access ecosystem.

Firstly, there is a considerable risk that localization harms the global supply chain, making it less resilient and robust and ultimately undermining global access.[8,93] Global supply chains are increasingly complex; there are different stages—manufacturing raw materials such as active pharmaceutical ingredients (API or precursor chemicals) for therapeutics, formulation and packaging, and filing—to ensure the efficient and cost-effective production of quality health products and technologies. The growing complexity of different kinds of health products necessitates specialization of manufacturing facilities and workers, with multiple suppliers across global locations being used in many medical products, devices, and other technologies. The proliferation of localization efforts could disrupt these dynamics and ultimately undermine supply and prevent access.

A key reason that some global health experts are advocating for localization is to ensure pandemic preparedness and strengthen the security of supply during public health emergencies. However, even if localization policies were to successfully increase supply in non-emergency contexts, this does not mean that it will improve pandemic preparedness. Localization alone would not have addressed the complex problems occurring during the COVID-19 pandemic. The supply shortages that occurred during the COVID-19 pandemic were unprecedented because global demand very suddenly exceeded supply. Even when there was supply, many countries lacked the necessary health infrastructure and policy framework to distribute and vaccinate their populations.

The strain that global health emergencies place on the raw materials for health products and technologies, such as APIs and medical device/diagnostic components, means that access to these components via the global supply chain is likely to be the major bottleneck for improving access during these times, rather than the level of local manufacturing capacity. For example, during the pandemic, restrictions put in place by governments, including lockdowns, shipping bans, border closures, and travel bans, contributed to severe shortages of raw materials used to manufacture many critical health products and technologies. In fact, some pharmaceutical manufacturers had to halt production as inventories fell.[95,96] Without ensuring resilience measures for the upstream supply chain of APIs and other raw materials, localization is unlikely to improve supply security during emergencies nor improve pandemic preparedness.

Another reason why some argue for localization is the belief that, during health emergencies, local production facilities can be repurposed to ramp up the supply of health products if the global supply chain is challenged. While it may be possible for companies to switch or repurpose production lines to ramp up manufacturing of certain health products and technologies,[97] it is not always easy or even possible to switch production from one facility or manufacturing line to another.[54] For example, it was estimated that only 1 to 5 percent of existing subunit and viral vector vaccine manufacturing capacity globally could be repurposed to expand the production of COVID-19 vaccines.[98] Given repurposing of production capacity may not be possible during an emergency response, ensuring the resilience of the global supply chain becomes even more important. Regional manufacturing efforts need to be integrated into global efforts to deliver efficiencies and ensure agility. Integration of all regions into the broader global supply chain as partners is critical for equitable access.

Box 7: Case studies highlighting the limited scope of localization policies

Brazil

In 2009, Brazil introduced policies that facilitated technology transfer for local production and provided a price premium for locally produced technologies. These localization policies were intended to stimulate the local industry and ensure the supply of pharmaceuticals. However, these policies did not address the major barriers to accessing health products and technologies in Brazil, which included a high reliance on out-of-pocket spending and a sub-optimal level of healthcare infrastructure.[99] While there have been some improvements in the availability of some products like generic medicines, many access challenges and high unmet needs persist.[100]

India

India has been implementing localization policies to increase the availability of vaccines since 1985. Despite this, numerous barriers, including an insufficient number of healthcare workers, an immature regulatory system, high levels of OOP expenditure, and vaccine hesitancy, especially in rural areas, prevented any increase in vaccinations. Deaths from vaccine-preventable diseases remained high.[86] However, in 2011, as part of the Pulse Polio Programme, India successfully eradicated the Wild Polio Virus by increasing access to the Oral Polio Vaccine. This increase in access was facilitated by a package of policies, including campaigns by local leaders to minimize the social concerns underlying vaccine hesitancy, large-scale training to increase the number of health workers qualified to administer vaccines, providing vaccines free of charge under India's Universal Immunization Programme, and developing the necessary cold-chain infrastructure. Despite India's localization policies, the Oral Polio Vaccine used in the Pulse Polio Programme was imported, demonstrating that localization does not necessarily have to be included in a package of measures to increase access.[101]

To improve access to health technologies, countries must address barriers across the access ecosystem and put forward a set of appropriate policies.

Equitable access to health products and technologies depends on multiple access drivers, as set out in the previous chapter. Multiple barriers often prevent access to health products and technologies. Therefore, to improve equitable access to health products and technologies, a package of policies is needed that optimizes the access ecosystem across all the drivers.

We can learn from the experience of several countries where localization policies have been implemented but as part of a package of policies. For example, we can contrast the case study of India with that of Brazil (Box 7).

In Brazil, although there has been a policy of localization, it was a standalone initiative, and the evidence is that access to health products and technologies has largely been unchanged.[100] In India, the challenge of improving access to the Oral Polio Vaccine was considered holistically with a focus on healthcare capacity, funding, and awareness.

Often, localization policies focus resources on promoting finished goods manufacturing. The existing evidence suggests there are often unsuccessful (for reasons noted above), resulting in inefficient use of resources and also neglecting opportunities to participate in supply chains for intermediary products. There is a legitimate concern that non-viable and non-resilient localization efforts will lead to wastage of resources that could instead be used to strengthen the access ecosystem.

Summary

Based on an examination of past programs and policies, localization policies alone are unlikely to improve access. The drivers of the access ecosystem represent the necessary enablers of access regardless of whether health products and technologies are supplied from local, regional, or global production. Localization and regionalization purportedly seek to improve the supply availability of health products and technologies but leave most access barriers unaddressed.

- Evidence from prior attempts at localization shows that, although intended to improve supply, it can instead undermine supply and hinder access by disrupting critical parts of the access ecosystem, such as the supply chain. For example, further fragmentation of the global supply chain can strain the availability of raw materials and other development and manufacturing inputs.

- Policies that require or force localization can damage access by restricting the international supply of health products and technologies when the ecosystem does not support a viable and sustainable local supply. Many countries lack the necessary human resources and specialized infrastructure to manufacture many health products and technologies.

- Local production of health products and technologies is primarily designed to only address supply availability. However, supply availability itself is only one component of the access ecosystem, and therefore, its impact on patient and consumer access is limited. Further, localization can only address supply availability under very specific circumstances (e.g., when there is sufficient market size to develop economies of scale and sustain demand).

- Localization raises the cost of health products and technologies because it increases the cost of goods (COGs) by decreasing the economies of scale for global supply chains. Local manufacturers often struggle to compete with foreign competitors due to their high prices.

- Localization alone would not have addressed the problem occurring during the COVID-19 pandemic. The supply shortages that occurred during the COVID-19 pandemic were unprecedented because global demand very suddenly exceeded supply. Even when there was supply, many countries lacked the necessary health infrastructure and policy framework to distribute and vaccinate their populations. High-income countries largely adopted an insular approach, driven by health and national security considerations, which resulted in vaccine “hoarding”, exacerbating supply shortages in LMICs.

- Often, localization policies focus resources on promoting finished goods manufacturing. These are often ultimately unsuccessful (for reasons noted above), resulting in inefficient use of resources and also neglecting opportunities to participate in supply chains for intermediary products.

- Policies that result in investment in non-viable and non-resilient localization efforts could lead to wastage of resources that could instead be used to strengthen the access ecosystem. However, regionalization could be a meaningful contributor to access if supported by an enabling framework.

However, regionalization could be a meaningful contributor to access if supported by an enabling framework.

- Regionalization can only contribute to improving access on a sustained basis if done with a holistic approach. Relative to country-level localization, regionalization has the advantage of creating a larger potential market, which could allow producers to capitalize on economies of scale and production efficiency. To achieve this, regionalization efforts need to be coupled with supportive policies at both national and regional levels, such as regulatory harmonisation, cross-border trade, advance purchase agreements, and regional supply chain infrastructure and distribution networks. However, maximizing economic efficiency will require supply chains to be global in nature, and end-to-end manufacturing will typically not be possible within a single region.

- Regional manufacturing efforts need to be integrated into global efforts to build efficiencies and ensure agility. Integration of all regions into the broader global supply chain as partners is critical for equitable access.

- In terms of pandemic preparedness, regional manufacturing efforts may still be strained during global health emergencies when specific raw materials, such as APIs and manufacturing inputs for medical devices and diagnostics, are in disproportionately high demand. Access to these components via the global supply chain is likely to be the major bottleneck for improving access during these times, regardless of the level of regional manufacturing capacity. In addition, efforts to source regionally, even at a larger scale, may risk undermining wider supply, reducing resilience gained through diversification.

Recommendations for policymakers

Drawing on the experience set out in Chapter 4, we present recommendations regarding the policy changes needed to improve equitable access to health products and technologies. These recommendations are intended to be viewed holistically rather than individually.

Policymakers and the global health community should focus on introducing a supportive package of policies and initiatives that target the whole access ecosystem—addressing access barriers, securing supply, and strengthening healthcare systems.

To sustainably improve access to all forms of health products and technologies, policymakers and the global health community should focus on introducing a comprehensive set of measures to address access barriers, secure supply, and strengthen healthcare systems. The access ecosystem needs to be viewed holistically, and resources deployed to address multiple barriers. Where resources are limited, efforts could be concentrated on the largest barriers within a given country to produce incremental gains in access.

Policies to achieve this at the national level should include, but not be limited to, the following:

- Implementing efficient regulatory mechanisms by adopting regulatory reliance and recognition, digitalization of regulatory processes, and regulatory convergence to international best practices and standards.
- Addressing trade barriers and supply chain bottlenecks through measures to ensure the free flow of products across borders, and efforts to improve infrastructure and facilities for receiving, storing, distributing, and administering different types of health technologies.
- Optimizing healthcare funding, infrastructure, and workforce by increasing national health budgets and introducing efficiencies in spending to improve health service delivery for patients and reduce out-of-pocket (OOP) payments.
- Leveraging value-based procurement criteria that consider not only price but also quality, supply resilience, competition, and value to patients, healthcare systems, and society.
- Strengthening intellectual property (IP) protection mechanisms to international standards to increase access to innovative health technologies.

- Improving demand forecasting and generation through the development and regular update of clinical guidelines and the use of health information systems.

- Improving awareness and health literacy of the population to facilitate uptake of available health products and technologies.

Supportive policies also need to be implemented regionally to foster regional collaboration, including but not limited to the following:

- Regulatory convergence: Regional harmonization of regulatory requirements that adhere to international standards and best practices, reducing unnecessary, redundant reviews and the burden on regulatory authorities.

- Purchase agreements and minimizing trade barriers: Governments in a region can improve the viability of a sustainable regional market by reducing regional trade barriers and creating an open market (discouraging forced localization policies that hinder trade). Furthermore, governments and other procurers need to commit to supporting market formation within a region through advance purchase agreements.

- Supply chain optimization: Strengthening regional supply chain infrastructure, processes and distribution networks, and facilities to ensure countries can receive, store, distribute, and safely administer health products and technologies. In addition, there is a need to strengthen the resiliency of the upstream supply chain of APIs and other raw materials to ensure supply security, particularly during health emergencies.

- Fostering new collaborations: There is a shared desire to improve equitable access. Manufacturers who export globally have a unique perspective on how to improve supply sustainability and to achieve the objectives articulated by policymakers. Their role in the exceedingly complex global supply chain (with individual companies working together at unique points in the value chain and across many countries) makes engagement and knowledge sharing critical to ensure sustainability. Policymakers need to foster new collaboration across global health actors in the public and private sectors to ensure investments and policies are aligned with sustainable access and avoid unintended consequences.

The goals of localization can be met by addressing the barriers to access.

Localization (or regionalization) alone is unlikely to improve access on a sustained basis. Localization as a tool to improve access only attempts to address the availability of supply and supply-chain issues, leaving many access barriers unaddressed.

Some forms of localization, such as forced localization, are particularly problematic. Other forms, such as regionalization, can address concerns about market size, meaning that it is possible to exploit economies of scale but still do not address the multiple barriers affecting patient access.

By introducing policies to address barriers to access, policymakers can simultaneously improve access and foster the development of a local health technology industry by incentivizing global and local manufacturers to invest in innovative activities.

Annex 1. List of acronyms

AfCFTA	Africa Continental Free Trade Agreement
API	Active pharmaceutical ingredients
ATMP	Advanced therapeutic medicinal product
AVMA	African Vaccine Manufacturing Accelerator
CHE	Current health expenditure
COGs	Cost of goods
EDL	Essential Drug List
FDI	Foreign direct investment
GDP	Gross Domestic Product
HIC	High-income country
HTA	Health technology assessment
IP	Intellectual property
LMICs	Low- and middle-income countries
MA	Marketing authorization
NHM	National Health Mission (India)
NRA	National Regulatory Authority
OECD	Organisation for Economic Co-operation and Development
OOP	Out-of-pocket
PAHO	Pan American Health Organization
PAVM	Partnerships for African Vaccine Manufacturing
PHAHM	Platform for Harmonized African Health Products Manufacturing
PPD	Partnership for Productive Development
PPP	Public–private partnership
P&R	Pricing and reimbursement
R&D	Research and development
SUS	Sistema Unico de Saude
UHC	Universal health coverage
WEF	World Economic Forum
WHO	World Health Organization
WTO	World Trade Organization

Annex 2. Description of drivers of access

Industrial policy

Industrial policy refers to the laws and provisions of governments that impact economic activities, either for individual industries or industry as a whole. For health products and technologies, this can include policies that impact all stages of the value chain, including research and development (R&D), manufacturing, and supply. Industrial policy covers a broad range of mechanisms—some of which are assessed in this report—so it is impossible to generalize what is needed to improve access. However, industrial policy is an important driver of access as it shapes the decisions made by companies to invest, manufacture, and distribute health products and technologies in a country. Well-designed industrial policy is needed to support the predictability, efficiency, stability, and sustainability necessary to attract investment and thereby improve access to healthcare.[102]

Regulatory system

An efficient regulatory system is required to ensure that the development, manufacturing, marketing, and use of health products and technologies meet the necessary safety and efficacy levels to provide patients with high-quality products. Without regulatory approval, health products and technologies cannot achieve market access and, consequently, are not available for patient access. Delays in regulatory approval subsequently delay patient access.

Regulatory harmonization across a region facilitates pharmaceutical companies' submission of a single set of dossiers to several different countries, thereby reducing costs, time, and effort. The greater the regulatory harmonization within a region, the more attractive it becomes for investment as greater economies of scale are created.

Legal and intellectual property (IP) protection

Legal and IP protection concerns the extent to which patent applications, patents, trade secrets, and other forms of intellectual property are defended according to international guidelines, such as the term of patents, term extension provisions, and patent linkage requirements.[103] Although the literature on the impact of IP protections on access to medical technologies (particularly innovative medicines) is varied and complex, it is often noted that insufficient IP protections can stymie access to innovative technologies.[104] If a market has little protection from off-patent copies, there is little incentive to create, develop, and distribute a health technology. However, while weakening protections and their enforcement could be a barrier to the development of patented technologies in LMICs,[58,105,106] there is little evidence that strong IP protections are a barrier to access to health products and technologies in LMICs.[107,108]

Trade policy

No single country can be entirely self-reliant in obtaining health products and technologies for medical care or the necessary intermediate products. Most countries rely heavily on imports obtained via the global health supply chain.[40] Therefore, open trade policies are important for ensuring patients have access to health products and technologies. A restrictive trade policy (including the use of tariffs), which, among other practices, imposes high tariffs on imported health products and technologies, will raise the prices of imported products and decrease patient access through price inflation or decreased availability.[41] In recognition of this, the World Health Organization (WHO) and World Trade Organization (WTO) recommend that no taxes or tariffs be implemented for health products and technologies, and this has been put into practice by many countries (particularly HICs). However, a large number, mainly LMICs, continue to impose duties on health products, constituting a major obstacle to improving access.[46]

In addition to tariffs, other trade barriers, such as non-tariff measures, including export restrictions, create a huge barrier to access, as witnessed during the pandemic. From January 2020 to April 2021, more than 220 actions were taken by countries banning or limiting the export of certain products, for COVID-19-related reasons.[45] Some countries imposed export controls on vaccines or on inputs necessary for production, which hindered the production and equitable distribution of COVID-19 vaccines as well as therapeutics.[42,109] The economic impact of export restrictions has also been documented. The general conclusion is that export restrictions can negatively impact the global economy, affecting both the level and volatility of supply and prices. They can also lead to retaliatory measures that further prevent countries from accessing essential supplies, disrupt supply chains, and create uncertainty.[45]

Supply chain management

One of the key drivers of access is a robust, timely, and resilient supply chain from manufacturers of health products and technologies to patients. Manufactured health products and technologies are often produced within international supply chains where individual companies specialize in specific steps of the production process. An increasing number of products (particularly diagnostics and medical devices) comprise parts and components with various geographical origins. This shows the critical significance of global supply chains and international trade in ensuring the optimal flow of raw materials and finished products through global production networks.[40] While diversifying or decentralizing supply chains may help mitigate the impact of geopolitical risks to supply in some cases, increasing the number of manufacturing sites usually comes with higher production and supply chain costs and puts additional strain on global supply chains.

Health workforce

The health workforce consists of all individuals involved in the delivery of health services and the operation of healthcare facilities. To drive access to health products and technologies, the health workforce needs to be adequate, well-trained, and fairly distributed. The availability and accessibility of health products and technologies is strongly linked to the density and distribution of healthcare providers.[58,110] Highly trained specialists are often required to administer complex and highly innovative health products and technologies such as advanced therapy medicinal products (ATMPs) and high-tech medical devices. Other technologies, such as high-tech diagnostics, require specially trained health workers to make them accessible to patients. The WHO has set a global requirement of 4.[45] core health workers (defined as physicians, nurses, and midwives) per 1,000 people in order to administer essential health services, such as ensuring equitable access to health products and technologies.[111] In 2020, there was a global healthcare worker shortage of 15 million.[65,74] This constitutes a major access barrier globally, particularly in sub-Saharan Africa.[66]

Health financing and funding

Health financing is a core function of health systems that can enable progress toward universal health coverage by improving effective service coverage and financial protection.[107] In the absence of carefully designed health financing policies, healthcare costs, particularly when paying OOP, become a strong access barrier.[56]

A sufficient level of funding is critical to ensure the supply and uptake of health products and technologies. The level of funding and investment directly impacts the healthcare resources available to the population. For example, government funding is required to provide public health insurance coverage to

make healthcare more affordable, train more healthcare professionals, purchase more equipment, and acquire and deliver novel health products and technologies.

Health system infrastructure

Funding is a prerequisite for investment in the health system infrastructure, including hospitals and medical equipment. This can particularly impact diagnostics and medical devices, as they are not designed for implementation in the suboptimal laboratory conditions found in some LMIC settings.

Pricing, reimbursement and procurement mechanisms

Procurement mechanisms, including pricing and reimbursement (P&R) policies, determine which health products and technologies are available to patients in each country. There are a variety of pricing policies that drive P&R processes and procurement practices, including value assessment mechanisms such as health technology assessment (HTA) to determine price points; direct price control such as reference pricing; targeted public subsidies, for example, affordable health technology schemes; and purchasing policies like tendering and pooled procurement. The appropriate form depends on the type of technology. Approaches that fairly determine value, that are transparent in the process, that manage affordability, and have flexibility are seen as improving access to patient-centric, high-quality, and affordable health products and technologies, and enable value-based healthcare.[52,112] In reality, there is limited use of HTA and other value-based approaches in LMICs.[53,113] In many LMICs, popular policies for procuring health products and technologies include winner-takes-all-price-only tenders, which have significant risks, including concerns around quality and supply resilience.[114,115]

Clinical guidelines

Most health products and technologies require the involvement of healthcare professionals, and therefore, the rules determining their actions are an important determinant of access. Clinical guidelines are protocols that include recommendations intended to optimize patient care.[116] Prescribing patterns of healthcare providers are generally influenced by the availability of clinical guidelines, and access to health products and technologies can be facilitated by the availability of treatment guidelines to help providers make evidence-based decisions in clinical management and use of health products and technologies. In most LMICs, there is a paucity of well-designed treatment guidelines, which could undermine access to certain health products and technologies.[60]

Awareness and health literacy

Awareness refers to a patient's perception of a health technology, encompassing factors such as their health education.[117] The willingness of a potential patient to interact with the healthcare system and follow the advice of a healthcare provider may be affected by their awareness of any stigma, or negative perception, associated with accessing certain health products and technologies.[61] A lack of disease awareness can be a key barrier to health-seeking behavior and access to health products and technologies.[118] If there is a lack of understanding of disease patterns and the role that health products and technologies can play in treatment, then overall adherence, rational product use, and disease management are likely to be impeded.[119] During the COVID-19 pandemic, vaccine hesitancy was a significant barrier to the uptake of COVID-19 vaccines in many countries (LMICs and HICs).[63]

Annex 3. Case studies

Algeria

Access barriers

Algeria's health sector strongly focuses on guaranteeing free access to healthcare. The public health system offers near-universal coverage, health services that are free at the point of delivery, and out-of-pocket payments have fallen to a low share of total health spending (around 20 percent).[120] In terms of health products and technologies specifically, most patients receive public reimbursement, with 85 percent of outpatient care covered by social security and about 80 percent of the cost of health products and technologies covered by the El Chifa card. However, due to import bans, innovative products are not allowed into the country unless they are locally produced.[8] Shortages across different types of health products and technologies have been consistently reported.[121] The following drivers of access are the most prominent challenges:

- Supply chain management: There have been shortages of health products and technologies across the supply chain. This can partly be attributed to the complexity of the actors involved (over 600 wholesalers are registered), but there is no robust real-time information system for monitoring the quantities available throughout the distribution chain. In 2019, the Ministry of Health, Population and Hospital Reform introduced several measures to address shortages, including establishing a monitoring unit and supplementary import programs even where domestic products should be relied on under trade policies. However, shortages have continued to be reported.[122]
- Health system funding and infrastructure: Algeria spends less than 5 percent of its GDP on healthcare. While the public health system offers broad coverage of the essential medicines reimbursed, access to innovative health products and technologies remains very difficult due to the limited willingness to pay and cost containment issues in the public system, and innovative medicines are perceived as very expensive.[123] This means that reimbursement of new health products and technologies is limited.[124] There is a significant geographical disparity (between the North and South of Algeria) in the availability of health infrastructure and workforce, which could be undermining access to health products and technologies in underserved areas.[125]

These access barriers help explain why Algeria's localization policies have not helped to improve access in the country.

Localization policies and their impact on access barriers and access

Algeria's localization policies for medicines began in 2008, when the first restrictions on drug imports were introduced.[7] Specifically, the regulation stated that a foreign-manufactured medicine cannot be imported if the same medicine is produced locally by at least three manufacturers in quantities satisfying demand. This has undergone several revisions, with over 300 products listed as excluded from import.[7] Another key policy has been the "51/49" rule, which limited multinational corporations to 49 percent ownership in foreign direct investment (FDI) projects (FDI related to complex and protective technologies for innovative products was exempt)

from 2009 until the relaxation of the law in 2020.[126] More recently, the Ministry of Pharmaceutical Industry (MOPI) was formed in 2020, with one of the objectives being to localize drug production. In Algeria, the primary aim of localization has been to spur the development of the local pharmaceutical industry, and the government aims to gradually reduce imports and boost local production. While not a primary objective, greater local production should reduce the cost of medicines and support availability.

In Algeria's case, the primary objective of localization policies—to spur development of the local pharmaceutical industry—has broadly been achieved: local pharmaceutical production increased from 40 percent of the total market in 2011 to over 70 percent in 2021, meeting a key strategic target of the government.[127] Algeria now has some 200 production units, which cover nearly 70 percent of its generic needs, with both multinational (e.g., Sanofi, Novo Nordisk, and Pfizer) and local (e.g., Saidal, Biopharm) companies establishing manufacturing sites.[128]

Notably, the experience of manufacturers is that the localization policies themselves may not have been sufficient for these companies to invest in local production; instead, pharmaceutical companies cite the extensive social insurance system as a driver of investment in Algeria.[129] In other words, improvement in the healthcare system encouraged localization, ensuring greater access (rather than the other way around).

Looking at the role of localization in addressing the access barriers, increased local production of health products and technologies (particularly medicines) has not contributed to improved access. In fact, there is evidence that one of the key barriers —Algeria's supply chain for medicines—has been further hindered by localization: as there are insufficient resources and infrastructure for producing some medicines, shortages of some 320 mainly chronic disease treatments were reported in 2015. Many of these had been recently added to the list of banned imports but have not yet been supplied by local manufacturers.[7] Algeria's localization efforts might have reduced the prices of generic products and improved their availability, but the same cannot be said of innovative and more complex products. A recent analysis showed that only 2 percent of new medicines launched globally from 2012 to 2021 were available in Algeria.[124]

Brazil

Access barriers

As part of implementing the Sistema Unico de Saude (SUS) since the 1980s, Brazil made notable progress in the 1990s and 2000s in expanding access to healthcare. Between 2002 and 2017, the list of essential medicines and medical products grew from 327 to 869.[99] The Popular Pharmacy Program (Farmacia Popular), initiated in 2004, expanded access to medicines, with subsidized prices and low copayments, and by 2010, progress towards achieving the SUS's objectives of universal health coverage was extensive. Despite this progress, however, several key challenges remain, and these reforms did not fully address structural weaknesses in the health system. Recent analyses of the access barriers to medicines and other health products and technologies with the SUS revealed supply chain bottlenecks resulting in low availability of medicines in SUS pharmacies.[130] Inequalities in unmet needs for both healthcare services and medications, with a primary impact on the poor, have also been reported.[100]

The following access barriers were identified as prominent in Brazil:

- Supply chain management: Despite the introduction of stricter monitoring and quality control in Brazil's supply chain management system in 2016, shortages of health products and technologies persist, with intermittent stock delivery forcing rationing of health products. Furthermore, due to supply chain bottlenecks, about 40 percent of medicines prescribed in public primary healthcare are unavailable when needed.[131]
- Legal and IP protections: Key challenges include patent backlogs and lack of regulatory data protection for pharmaceutical products. In recent years the Supreme Court revoked the sole paragraph of Article 40 of the Brazilian Industrial Property Law, doing away with a 10-year minimum of patent protection, and new legislation was introduced allowing the government to grant compulsory licenses more easily (including compelling transfer of technology and know-how).[132]
- Health system funding and infrastructure: Although SUS enabled an expansion of universal health coverage (UHC), the healthcare system is limited by low public financing, with government health expenditure at 4.6 percent of GDP.[133] There has been a decrease in per capita spending in real terms since 2015.[69] A recent Constitutional amendment imposing a public spending ceiling will decrease access for patients.[99] Around 90 percent of pharmaceutical spending is financed by private insurance and OOP payments, constituting a major barrier to access. Gaps in coverage of health products and technologies remain an important issue that affects poor and disadvantaged people disproportionally. Sub-optimal levels of healthcare infrastructure, such as a low number of hospital beds, especially in rural areas, is also a barrier to access in Brazil, with only 2.5 beds per 1,000 people.[134] This is particularly a huge challenge in regions with high poverty rates. There are weaknesses in the country's health information infrastructure. Brazil lags behind OECD countries in data availability, reporting, governance, and integration.[135]

- Health literacy: Health literacy appears to be a particular concern in Brazil, limiting access to health products and technologies, even when technologies are affordable and available. Studies show that 31.7 percent of Brazilians are health illiterate, and only 18.7 percent of patients fully understand their prescriptions, leading to patients failing to access the health products they have been prescribed.[136,137] Overall, 53.9 percent of Brazilians display inappropriate use of health products and technologies due to a lack of awareness.[119]

Localization policies and their impact on access barriers and access

Localization policies for medicines in Brazil have been introduced primarily within more general economic and industrial policies to support the local industry. One notable policy, introduced in 2012 for numerous industries, is the 'margin of preference' for acquiring certain medicines in public tenders conducted by the federal government. This policy provides a price premium of up to 25 percent for medical technologies in government contracts produced locally.[8] Other key policies have been Decree 8304 (2014), which introduced local content requirements to quality for export assistance and provided a 3 percent subsidy for pharmaceuticals with less than 65 percent of inputs imported, and the Partnership for Productive Development (PPD), a program introduced in 2009 to foster knowledge sharing and technology transfer for local production.[7] These policies are primarily aimed at stimulating the production and competitiveness of domestic industries—for example, the pharmaceutical sector is only one of the numerous industries with a margin of preference—with access generally not a focus. Nonetheless, ensuring quick supply and reducing prices have been reported as secondary objectives.[138]

Despite these policies, there is a mixed picture of whether localization has achieved its primary objectives of stimulating the competitiveness of domestic industries and reducing dependence on the international market. Instead ofreduced dependence, Brazil's trade deficit in pharmaceutical goods increased from around US$2 billion in 2011 to over US$3 billion in 2017 and US$7 billion in 2022 (though impacted by imports related to COVID-19).[132,139] Up to 95 percent of pharmaceutical manufacturing depends on imported active pharmaceutical ingredients (APIs), and localization policies have certainly not improved API manufacturing.[140]

Looking at the role of localization in addressing the access barriers, Brazil's levels of access to medicines do not seem to have changed over the period in which localization was implemented. Although Brazil currently offers universal healthcare coverage, 3.8 percent and 7.5 percent of the population reported unmet needs for healthcare services and medication, respectively, in a 2019 survey.[100] Moreover, the percentage of the population experiencing unmet needs, specifically for medicines, remained unchanged between 2013 and 2019.

The lack of any tangible impact on access can be explained by the fact that localization alone could not address the root causes of lack of access, particularly the underlying challenges in health system funding. Indeed, the proportion of people not obtaining medicines from the public system is increasing, and there is high reliance on private spending (4.4 percent of the 8.2 percent of GDP spent on health).[100] Although there has been a slight increase in the launch of new medicines—from 33 percent in 2017 to 37 percent in 2021 of all new medicines launched globally, which is higher than the regional average of 29 percent—this is more likely to have been driven by predictability in the regulatory system.[124,139] Finally, a key challenge remains the persistence of stark geographical inequalities, which localization is unlikely to address.

India

Access barriers

The Indian government launched the National Health Mission (NHM) in 2005 to increase equitable access to affordable and quality healthcare, including access to health products and technologies. It was initially focused on rural populations but expanded to urban areas in 2013.[141] NHM has successfully addressed barriers to equitable access, including introducing new technology and consistent checkpoints for a more responsive and reliable supply-chain system.[142] Despite this progress, several key challenges remain, and there are stark geographical inequities in access to medicines. Access to essential medicines in India is estimated at below 35 percent,[143] with the following access barriers identified as most prominent:

- Regulatory system: India's regulatory system is not sufficiently strong to enforce health technology regulations, particularly in addressing production and circulation of sub-standard health products.[144] Reports suggest that 3–4 percent of drugs produced in India are substandard, and an investigation into the quality of cough syrups produced in India found that 6 percent were not of sufficient quality.[145,146] It should be noted that the regulatory system for vaccines in India has improved since 2012, following government investment in capacity building.[147] In 2017, the NRA in India was designated at maturity level 3 (ML3) for vaccine regulation—a key milestone for India in producing vaccines that can be pre-qualified by WHO, therefore facilitating export via United Nations procurement.[147]

- Health system funding and infrastructure: One of the strong access barriers in India is inadequate government funding. Government expenditure amounts to only 1.1 percent of GDP,[69] below the WHO recommended figure of at least 5 percent.[148] This has implications for infrastructure, as there are only 0.5 hospital beds per 1,000 people, below the average of 2.3 hospital beds per 1,000 people in LMICs.[149] A study of six states in India found that many primary healthcare centers (PHCs) lack basic infrastructural facilities such as beds, wards, toilets, clean labor rooms for delivery, and regular electricity. The insufficient health infrastructure varies by region, but the high rural population in India means that 63 percent of the population cannot access inpatient healthcare facilities within 5km.[150]

- Health workforce: In 2020, India had 0.7 medical doctors and 1.7 nursing and midwifery personnel per 1,000 people, well below the WHO benchmark of 4.45 health workers per 1,000 people.[151] Once more, this shortage of healthcare workers is amplified in rural areas, with community health centers suffering an 83 percent shortfall of surgeons.[152] This limited health workforce and insufficient infrastructure for healthcare delivery and health technology storage is a major barrier preventing access to vaccines, especially in rural areas and densely populated slums.[153]

- Health financing: Substandard government funding also forces high OOP expenditure. In 2021, the estimated UHC in India was 63 percent.[154] This means that many patients seeking to access health products and technologies would often have to pay out OOP, to the extent that 49.82 percent of health expenditure in India was OOP in 2021.[155] As a result, impoverishing OOP, otherwise known as catastrophic health expenditure, in India is 4.17 percent, with many patients and households having to decide between accessing health products and technologies and falling further into poverty, making it the biggest barrier to equitable access.[156]

The high number of access barriers in India underlines an access ecosystem that prevents equitable access to all health products and technologies. Therefore, any success localization policies could have in boosting local manufacturing and increasing supply would have a limited impact on improving access without addressing the other factors that make up the ecosystem.

Localization policies and their impact on access barriers and access

Since the 1980s, India has implemented a package of localization policies aiming to improve the local manufacturing capacity for specific health products and technologies. For example, the Universal Immunization Program (UIP), launched in 1985 to reduce the child mortality rate from vaccine-preventable diseases, introduced localization policies that forced vaccines to have local manufacturing capacity in order to be included in the Program.[86] This forced policy was implemented alongside incentivized localization that looked to create an enabling environment for local production:

- In 1986, the Department of Biotechnology (DBT) was formed to support local manufacturing companies, including setting aside specific government funds to invest in developing vaccine R&D in India.[157]

- In 1989, the Indian government set up special economic zones. These were treated as foreign territories regarding trade and tariffs, incentivizing international manufacturers, such as Pfizer, to establish local manufacturing facilities.[158]

- In 2004, the Indian government established the Pharmaceuticals Export Promotion Council of India (Pharmexcil) to facilitate the export of locally produced products.[159]

- In 2004, the DBT established the Biotechnology Industry Research Assistance Council (BIRAC) to support local manufacturers seeking to provide affordable health products and technologies that are highly demanded in India.[160] In 2017, BIRAC invested $250m to establish the National Biopharma Mission (NBM), which encourages companies to 'Innovate in India' through projects such as providing guidance to support vaccines through pre-clinical and clinical stages of development, offering attractive clinical trial guidelines, and developing regional hubs that provide a streamlined regulatory process for local vaccine manufacturers to bring products to the market.[161]

- In June 2020, the Department for Promotion of Industry and Internal Trade amended its 2017 Public Procurement Order, giving priority to Indian companies whose products contain 50 percent or more local content. Products with less than 20 percent local content are categorized as "non-local suppliers" and cannot participate in government tenders.[162] For healthcare companies, government business is about 25 percent.[54]

Localization efforts in India have been a mix of different set of policies. Some of the policies incentivize localization while others force localization such as local content requirements. Despite these policies, the indigenous market size is the most important factor behind India's success in improving vaccine manufacturing capacity. Through the UIP, local vaccine manufacturers have a guaranteed market of ~25 million newborn children each year, allowing local manufacturers to develop economies of scale and provide lower prices than international competitors.[86]

Evidence suggests there has been some success in building local manufacturing capacity in India. As of 2023, India produces more than 40 vaccines that are prequalified by the WHO for international exportation and has the capacity to manufacture more than 8 billion doses per year.[163,164] In 2022, the UIP provided locally manufactured vaccines for 11 different diseases for over 25 million children.[165] This has had a quantifiable impact on childhood access to vaccines and has been a key driver in the decrease in under-five mortality rates from 45 per 1,000 live births in 2014 to 35 per 1,000 live births in 2019.[166]

However, any success in improving access has been built on the foundation of a package of policies that have looked to address the major barriers to access in India and make incremental gains in optimizing the access ecosystem. For example, the UIP provides vaccines free of cost and invested in cold-chain infrastructure to create 30,000 cold-chain points in 2022—overcoming some of the key barriers to access identified in India.[166] Similarly, the successful eradication of the Wild Polio Virus in India through the Pulse Polio Program occurred because policymakers introduced several policies to facilitate access to the Oral Polio Vaccine (OPV) for 900 million individuals.[101] These policies included tackling stigma by utilizing local leaders to minimize the social and cultural concerns underlying vaccine hesitancy and running large-scale training to increase the number of health workers who could administer vaccines. Despite the growth of local manufacturing capacity, the OPV was imported to India, once again highlighting localization's limited role in improving access.[101,167]

Several key access barriers also remain unaddressed by localization. For example, logistical issues such as supply bottlenecks and vaccine hesitancy prevented access to the COVID-19 vaccination, despite its high supply from local manufacturers. Until policies are put in place that target the ecosystem, including addressing inadequate health workforce and large geographical variations in infrastructure, access will not progress in India. Furthermore, a singular capability to manufacture vaccines may reinforce only this aspect of access to health; while a cervical cancer vaccine is attracting government resources, there remains no scaled effort to screen and treat women who may already have cervical cancer, where no local diagnostic for HPV[a] is available.

Furthermore, other access barriers have been exacerbated by the introduction of localization policies. Localization policies that intend to boost local manufacturing by raising import tariffs for internationally produced technologies often reduce access to technologies that cannot be manufactured within India. For example, in 2020, the import duty on medical devices was raised from 5 to 7.5 percent. Combined with inter-state Goods and Service Tax and health cess ad valorem, imported medical devices are often taxed at 25–26 percent of their total value.[168,169] Considering India's low healthcare coverage, this cost is often passed on to the consumer, and the high price acts as a barrier to accessing medical devices in India. Similarly, during the COVID-19 pandemic, poor trade policies prevented the export of the Indian-produced vaccine and prohibited importation when India faced shortages.[170]

a The HPV test looks for the presence of high-risk HPV which is known to cause about 99 percent of all cervical cancers.

Indonesia

Access barriers

Access to health products and technologies has advanced rapidly in Indonesia in the past decade. In striving to achieve universal healthcare coverage, the government introduced a national health insurance scheme in 2014, Jaminan Kesehatan Nasional (JKN). At the start of 2023, the JKN scheme had registered over 253 million participants, representing 93 percent of the population.[93] Despite this, expanding the supply of healthcare services to each of Indonesia's 7,000 inhabited islands has proved challenging, and this geographical challenge is the underlying foundation for the key barriers to further improving access that exist, including the following most prominent challenges:

- Health system funding and infrastructure: There is a low number of hospital beds per capita, and hospitals and bed capacities are not evenly distributed throughout Indonesia: in five provinces the number of hospital beds per thousand people is less than one.[171] There is a disparity in hospital utilization between urban and rural areas, with adults living in urban areas 1.3 times more likely to use hospital outpatient facilities than those in rural areas.[172] Despite the incentives for placement, less than 10 percent of physicians practice in rural communities, which make up 45 percent of Indonesia's population.[173]

- Health workforce: Although particularly pronounced regarding geographic disparities, shortcomings in the health workforce have generally been a key national challenge. The number of physicians and nurses may be as low as under half of the government's objective, and in 2015 only 53 percent of health centers had sufficient numbers of dentists, 75 percent had sufficient numbers of general practitioners, and 62 percent had sufficient numbers of midwives.[173]

- Health financing: Despite the health insurance scheme in place, the burden of out-of-pocket spending on treatment remains high in Indonesia. By 2017, although national insurance covered 70 percent of the population, only 18 percent of total services were covered, and out-of-pocket expenses remained considerable at 48.3 percent.[173]

Localization policies and their impact on access barriers and access

Indonesia's main localization policy was implemented in 2008: the Ministry of Health Decree 1010 prevents a company from gaining marketing authorization unless registered as a "local pharmaceutical industry."[8] To gain market access, foreign companies must establish local manufacturing facilities or transfer intellectual property rights to a local company. The stated goal of Decree 1010 was to protect patients from counterfeit and substandard medicines, with strengthening the domestic pharmaceutical industry frequently implied.[174] This policy sits alongside various other attempts to boost local industry, such as requiring local product prioritization over imports in government tenders, and the pharmaceutical industry is one of the five priority industries in the 2015–2035 National Industrial Development Master Plan.[174]

Since the implementation of the localization policies, local manufacturing growth has been significant. The pharmaceutical sector recorded 85 percent growth in 2007–2013.[91] Decree 1010 resulted in a predominantly local industry, with a 75 percent share.[92] Assessing the impact of localization on access is complicated in Indonesia, considering the extensive reforms to the health system in this period, particularly the UHC scheme in 2014. However, the availability of essential medicines appears to be higher in the period when the UHC scheme was being implemented than when only localization policies were in place. In 2014, a study assessing the availability of medicines revealed that more than 50 percent

of the drugs on the WHO-recommended Essential Drug List (EDL) were not supplied in the local market.[7] According to a more recent study in 2024, only 38 percent of essential medicines were not supplied in the local market. Furthermore, the study found that, under the JKN scheme, the median availability of 17 priority medicines was 82 percent, which is relatively high compared to other countries in the region.[93] Access policies, such as the JKN scheme, appear to improve the availability of essential medicines in Indonesia more than the localization policies.

Despite the complexity of assessing the impact of localization on access, it can nevertheless be reasonably stated that localization policies in Indonesia have not directly addressed the key barriers to access to health products and technologies: growth in local production has not addressed access issues in hard-to-reach and rural areas or the gaps in the Indonesian health workforce.

Singapore

Access barriers

Singapore is a different case as it is a HIC. As such, some access barriers are expected to be more likely addressed, given the availability of resources compared to LMICs. Singapore's health system is rated well in international comparisons. Although its health expenditure of 4 percent of GDP annually is still slightly below the often-cited benchmark of at least 5 percent, its overall health outcomes are comparable with many other HICs that spend significantly more on health.[175] In the context of health products and technologies, government subsidies are a major contributor to ensuring access to affordable and effective treatments for common medical conditions, while the MediShield Life national insurance scheme reduces the cost burden of treatments for inpatients and selected expensive outpatient treatments.[81] However, wider trends of a rapidly aging population and the rising burden of non-communicable diseases are stretching Singapore's health system and undermining access to healthcare.[176] In terms of trade, Singapore does not impose any tariffs on the import of technologies. Regulatory capacity is high as it is the world's first to achieve the highest ML 4 in the WHO classification of regulatory authorities for medical products. IP protection in Singapore is ranked one of the strongest in the world, currently above the international benchmark at 84.44 percent. Core health workforce density is also amongst the highest at 10.2 per 1000 people. A study conducted in 2021 found that health literacy is quite high, with 80.5 percent having high functional health literacy.[177]

However, despite the relatively strong access ecosystem in Singapore, there are a few access barriers that need to be addressed, including the following:

- Health system funding and infrastructure: From around 2011, there was growing concern as to whether Singapore's health system infrastructure had sufficient capacity, with perceived challenges including hospital bed shortages, overstretched medical staff, and long waiting times for available beds for patients admitted to emergency departments.[176] A key factor driving this growing challenge was Singapore's aging population, which was at least partly the reason why total annual hospital admissions grew by 23 percent between 2006 and 2015.[176] The Ministry of Health actively sought to mitigate these challenges with initiatives such as the Healthcare 2020 Masterplan, which included plans and targets for increased hospital beds and personnel capacity.[176]

- Pricing and reimbursement: The use of value-based assessment approaches for pricing and reimbursement of health products and technologies is well established but is mainly focused on informing subsidy decision-making and can be restrictive to newer health products and technologies, as evidenced by a recent analysis that shows that only 27 percent of new health products and technologies launched globally between 2012 and 2021 are available in Singapore.[81,124,178] Singapore needs to expand its HTA capacity beyond subsidy decision-making and facilitate greater access to newer health products and technologies in a sustainable manner.

- Health financing: Although for several decades the government has been establishing schemes to help patients pay for their share of medicines' costs, this challenge has never been wholly addressed. As recently as 2011, overall out-of-pocket expenses made up approximately 40 percent of total expenditure, compared to the OECD average at the time of 15 percent.[69] In 2015 the insurance coverage scheme was substantially enhanced to form MediShield Life,[176] and since that time out-of-pocket spending has fallen drastically to 19 percent of total health expenditure.[69]

Localization policies and their impact on access barriers and access

Singapore has a long history of supporting the localization of different parts of the industry value chain. Since 2000, Singapore has managed to shift its positioning from a pharmaceutical manufacturing outpost to a world-class location for biomedical activities across the whole innovation and manufacturing value chain with a strategic focus on value-add. Key features of this transition are shown in Figure 4. Singapore's biopharmaceutical sector has grown significantly by adopting this positive approach to attracting investments in developing its health technology ecosystem. From 2000 to 2019, biomedical manufacturing was the fastest-growing manufacturing sector. As of 2019, the biomedical manufacturing sector represented 20 percent of total manufacturing value added (S$19.57 billion), 4 percent of Singapore's GDP, and the number of manufacturing sites for biological drugs grew from 0 to 18 in less than 20 years.[8]

In fact, Singapore is now one of the few countries with a positive pharmaceutical trade balance: its exports of manufactured pharmaceuticals are more than twice the value of its imports.[80] Perhaps the clearest implication of Singapore's localization experience is the potential benefits of creating a positive wider ecosystem that supports investment into manufacturing rather than forcing companies to locate manufacturing sites there.

Access to health products and technologies has also improved significantly in Singapore, although there are still some challenges. Indeed, although only 27 percent of new medicines launched globally were found to be available there in 2022, this is much higher than the regional average of 20 percent.[124] However, attributing changes in access to the implementation of incentivized localization policies is made more challenging by the various other healthcare policies that have been implemented. Rather, according to interviews, the key drivers of access are much more likely to have been the government's national insurance schemes to increase the availability and affordability of healthcare. At the very least, it can reasonably be said that Singapore's localization policies do not seem to have hindered the development of its health system into one of the highest rated in the world.

Figure 4: Key investment areas in developing a sustainable export-driven manufacturing ecosystem in Singapore

Source: CRA analysis

South Africa

Access barriers

In 2009, the South African government announced a 10-point plan to reform the country's health system and improve equitable access to health products and technologies.[179,180] There has been significant progress in addressing some of the barriers to equitable access to health products and technologies, and the plan has been reinforced by an increase in government funding, with expenditure exceeding 5 percent in 2020 after trending upwards since the 2000s,[69] and South Africa does not impose tariffs on health products and technologies.[181] There has also been progress towards the 4.45 core health workers per 1,000 necessary to administer essential health services.[111,182] In 2019, there were 4.29 core health workers per 1,000 people in South Africa.[182] Despite this, a number of access barriers remain that prevent access to health products and technologies in South Africa:

- Supply chain: There is a high frequency of health technology stockouts, due to inefficient supply chain practice, with 86 percent of health facilities lacking complete availability of essential medicines in 2012.[183] Reforms have not adequately addressed this; poor supplier performance management was the most important barrier to medicine access in the Western Cape Province in 2017.[184] These concerns are exacerbated by rural inequalities. In 2013, stockout rates of medicines and vaccines in rural provinces were 54 percent and 35 percent, respectively.[183] There is an insufficient complement of skilled workers to manage the supply chain, resulting in supplier non-payment, poor supplier performance, and an inefficient tendering process.[185] In 2023, 37 percent of primary healthcare clinics did not have a pharmacy assistant, which increased the likelihood of an erratic supply of health technology.[186] The availability of skilled healthcare management and support workers decreased from 0.48 per 1,000 people in 2005 to 0.26 per 1000 in 2018.[187] Supply-chain inadequacies are perhaps the most significant barrier to equitable access to vaccines, with underlying reasons such as cold-chain and distribution issues.[188] In 2018, there was a 3-month stockout of the BCG vaccine due to distribution issues and shortages. In 2022, 2021, and 2019, there were stockouts of at least 1 month of the Oral Polio Vaccine. In 2019, 2018, and 2017, stockouts of the TT / DT / Td-containing vaccine ranged from 2 to 3 months.

- Regulatory system: Although the regulatory system has improved in South Africa since the establishment of the SAHPRA in 2018, it remains a crucial barrier to accessing health products and technologies.[189] For example, there are inadequate provisions to tackle the high prevalence of substandard and counterfeit medicines, and regulatory reliance has been limited to clearing a backlog of 160,000 applications that built up under the previous regulatory system.[30,190,191] Until recently, weaknesses in the regulatory system for vaccines, such as a long approval timeline, have been a major barrier to vaccine access. However, the recent ranking of South Africa's vaccine regulatory system as ML3 by the WHO in October 2022 signals progress in staffing, quality management, and the process of marketing authorization.[192]

- Health system funding and infrastructure: The quality of public healthcare facilities in South Africa has been consistently classified as 'at risk of failure' since 2006, and it is estimated to cost ~US$110 million to rectify.[193] There is also an inadequate number of healthcare facilities, with only 2.3 hospital beds per 1,000 people.[149] There is marked variation in the number of hospitals, number of hospital beds, and number of surgical-specific beds across geographical regions;

20 percent of poor rural households live more than an hour from the closest hospital due to the low number of 0.53 hospitals per 100,000 rural population.[194–196] In urban areas, rapid population growth has resulted in overcrowding, leading to a shortage of 1,347 beds across 26 public hospitals in Gauteng.[193]

- Awareness and stigma: Stigma associated with vaccination is a significant barrier to patient access in South Africa; the percentage of the population viewing vaccines as crucial for children in South Africa fell by 29.9 percent, to 62 percent, in 2023.[197]

Localization policies and their impact on access barriers and access

In an attempt to develop local vaccine manufacturing capacity to improve access to vaccines, especially during disease outbreaks, the South African government developed a public–private partnership (PPP) with the Biovac Consortium to create the Biovac Institute (Biovac) in 2003. Under the conditions of the PPP, Biovac was granted exclusivity as the sole public-sector vaccine supplier for the government's immunization program, under the condition that ~12 percent of a price premium be set aside to invest in developing local manufacturing capacity.[198] Through government investments and technology transfers with international vaccine manufacturers, the PPP has successfully generated a skilled workforce and improved vaccine infrastructure (see Box 8). However, Biovac's limited market size, contradictory government policies, and failure to address the key access barriers in the access ecosystem have prevented it from succeeding in improving the supply of vaccines in South Africa.[199,200]

Despite developing fill-and-finish capacity for PCV13 and DTaP-IPV-Hep B-Hib, Biovac has yet to formulate a vaccine from start to finish, and the localization policy has not had any tangible impact on access.[201] Access barriers in South Africa have prevented an increase in manufacturing capacity because the access ecosystem is not optimized. For example, SAHPRA only received ML3 for vaccines in late 2022[201]—this has delayed Biovac's progress in developing a vaccine from start to finish and also, alongside poor regional trade policies, prevented Biovac and Aspen Pharmaceuticals from exporting their locally produced COVID-19 vaccines to other African countries after they secured tech transfers with Pfizer/BioNTech and Johnson & Johnson, respectively.[202] This made Aspen Pharmaceuticals cease manufacturing their COVID-19 vaccine, at a point where 84 percent of the African population remained unvaccinated.[89]

This inability to export has prevented Biovac from generating economies of scale due to the low indigenous market size and uncertain demand in South Africa. As a result, locally manufactured vaccines are more expensive than internationally produced alternatives, and at the end of the procurement exclusivity agreement,[203] Biovac lost the competitive government tender to provide Pneumococcal vaccines for 2024–2026, losing to Cipla, an Indian-backed manufacturer offering its vaccine at approximately a third of the price of Biovac's.[83] This occurred despite the fact the government had invested significantly in building Biovac's capacity to formulate their pneumococcal vaccine from start to finish locally.[204–206]

Box 8: A timeline of Biovac

2003: Biovac is established[198]

The Biovac Institute was established, with the Department of Health holding a 47.5 percent share. A supply agreement with the South African Government granted Biovac exclusive procurement and distribution of vaccines for the South African Immunization Program.

2012: Biovac agrees a Tech Transfer with Sanofi for the vaccine Hexaxim[207]

Under the tech transfer, Biovac initially procured Hexaxim, a pediatric vaccine that prevents six childhood diseases. Input from Sanofi enabled Biovac to develop the capacity to manufacture the vaccine fully. This input was vital in Biovac achieving its 'Good Manufacturing Practice' in 2018 and SAHPRA approving Biovac for full manufacturing in 2020.

2015: Biovac agrees on a Tech Transfer with Pfizer for the vaccine Prevnar 13[207–209]

Under the tech transfer, Biovac initially completed 'fill-and-finish' on a pneumonia vaccine for infants. The tech transfer was then leveraged to develop the requisite capacity to produce the vaccine from start to finish. It was hoped this would improve affordability since the vaccine accounted for 40 percent of the government's total budget for vaccines in 2015. By March 2023, Pfizer had invested over R855 million in developing Biovac's manufacturing infrastructure, including aiding in building an 1100m^2 Freezer Farm Facility.

2019: Biovac loses its status as a PPP[210]

Biovac transitioned from a PPP to a joint venture between shareholders. This marked the end of the supply agreement and required Biovac to compete in tenders to supply vaccines to the government.

2019: Biovac wins 85 percent of tender for government's child vaccination program[211]

Despite concerns that the tender process would be prohibitive for Biovac, they secured a R9.7bn deal for vaccines, including Prevnar 13, from June 2020 to December 2023.

2021: Biovac agrees to a Tech Transfer with Pfizer to fill and finish their COVID-19 vaccination for supply to the African Union[212]

The tech transfer was announced in June 2021; following an accelerated tech transfer process, the first doses were produced in September 2022.

2021: Biovac announces as a key 'manufacturing spoke' in the new mRNA hub in Africa[213]

The tech transfer was announced in June 2021; following an accelerated tech transfer process, the first doses were produced in September 2022.

2023: Government changes tender criteria to allow lesser valent vaccines to compete, and Biovac loses tender to produce pneumococcal vaccines[205]

In April, Biovac lost out on the government tender for pneumococcal vaccines to the Serum Institute-backed supplier, Cipla. This development made Biovac lay off staff, leaving the future of local manufacturing uncertain.

Annex 4. References

1. World Local Production Forum (WLPF). Accessed February 1, 2024. https://www.who.int/initiatives/world-local-production-forum

2. Local Production for Access to Medical Products: Developing a Framework to Improve Public Health. Accessed March 12, 2024. https://www.who.int/publications-detail-redirect/9789241502894

3. A New Era of Vaccine Manufacturing in Africa. Accessed March 12, 2024. https://www.gavi.org/news-resources/knowledge-products/new-era-vaccine-manufacturing-africa

4. Potential measures to facilitate the productions of active pharmaceutical ingredients (APIs) | Think Tank | European Parliament. Accessed May 1, 2024. https://www.europarl.europa.eu/thinktank/en/document/IPOL_STU(2023)740070

5. European Health and Digital Executive Agency (European Commission), Gesundheit Österreich Beratungs GmbH, Tetra Tech, Vogler S, Salcher-Konrad M, Habimana K. *Study on Best Practices in the Public Procurement of Medicines: Final Report*. Publications Office of the European Union; 2022. Accessed May 1, 2024. https://data.europa.eu/doi/10.2925/044781

6. *Ordonnance N° 2018-1074 Du 26 Novembre 2018 Portant Partie Législative Du Code de La Commande Publique.*

7. Pugatch Consilium (2016). Separating Fact from Fiction – How Localization Barriers Fail Where Positive Non-discriminatory Incentives Succeed: A Global Assessment of Localization Policies and Incentivizing Life Science Investment and Innovation. Available at: https://www.pugatch-consilium.com/reports/Localization%20Paper_US_FINAL.pdf.

8. Localisation barriers to trade in the biopharmaceutical industry. Geneva Network. Published July 2, 2023. Accessed February 1, 2024. https://geneva-network.com/research/localisation-barriers-to-trade-in-the-biopharmaceutical-industry/

9. World Health Organization. Glossary of Health Systems Strengthening. Published 2011. Accessed June 13, 2024. https://cdn.who.int/media/docs/default-source/documents/health-systems-strengthening-glossary.pdf

10. Ten years in public health, 2007–2017. Accessed March 12, 2024. https://www.who.int/publications-detail-redirect/ten-years-in-public-health-2007-2017

11. Final Report. High-Level Panel on Access to Medicines. Accessed September 18, 2023. http://www.unsgaccessmeds.org/final-report

12. World Health Organization, World Intellectual Property Organization, World Trade Organization, eds. *Promoting Access to Medical Technologies and Innovation: Intersections between Public Health, Intellectual Property, and Trade*. 2nd edition. World Health Organization : World Intellectual Property Organization : World Trade Organization; 2021.

13. Overcoming obstacles to medicines access - Geneva Network - Access to Medicines | Barriers to Access to Medicines. Geneva Network. Published December 4, 2020. Accessed March 12, 2024. https://geneva-network.com/research/overcoming-obstacles-to-medicines-access/

14. Holloway K, Everard M. Equity in Access to and Quality Use of Medicines in Low- and Middle-Income Countries. In: *Encyclopedia of Evidence in Pharmaceutical Public Health and Health Services Research in Pharmacy*. Springer International Publishing; 2020:1-23. doi:10.1007/978-3-030-50247-8_135-1

15. Yenet A, Nibret G, Tegegne BA. Challenges to the Availability and Affordability of Essential Medicines in African Countries: A Scoping Review. *Clin Outcomes Res CEOR*. 2023;15:443-458. doi:10.2147/CEOR.S413546

16. CRA interviews with Global Health representatives. Published online November 2023.

17. Godman B, Bucsics A, Vella Bonanno P, et al. Barriers for Access to New Medicines: Searching for the Balance Between Rising Costs and Limited Budgets. *Front Public Health*. 2018;6. Accessed September 18, 2023. https://www.frontiersin.org/articles/10.3389/fpubh.2018.00328

18. Pharmaceutical Innovation and Access to Medicines | en | OECD. Accessed September 18, 2023. https://www.oecd.org/health/pharmaceutical-innovation-and-access-to-medicines-9789264307391-en.htm

19. Addressing challenges in access to oncology medicines - OECD. Accessed April 25, 2024. https://www.oecd.org/health/health-systems/addressing-challenges-in-access-to-oncology-medicines.htm

20. Science LS of E and P. Access to medicines in Europe: Delays and challenges for timely patient access. London School of Economics and Political Science. Accessed October 14, 2022. https://www.lse.ac.uk/business/consulting/reports/access-to-medicines-in-europe-delays-and-challenges-for-timely-patient-access.aspx

21. Mukherjee S, Goodman L. Strengthening regulatory systems globally: a crucial step towards pandemic preparedness and response. *BMJ Glob Health*. 2023;8(8):e012883. doi:10.1136/bmjgh-2023-012883.

22. Chisholm O, Critchley H. Future directions in regulatory affairs. *Front Med*. 2023;9. Accessed October 3, 2023. https://www.frontiersin.org/articles/10.3389/fmed.2022.1082384

23. Keyter A, Salek S, Danks L, Nkambule P, Semete-Makokotlela B, Walker S. South African Regulatory Authority: The Impact of Reliance on the Review Process Leading to Improved Patient Access. *Front Pharmacol*. 2021;12:699063. doi:10.3389/fphar.2021.699063

24. Improving the sustainability of the vaccine innovation ecosystem in Africa | Reports. Wellcome. Published July 13, 2022. Accessed March 13, 2024. https://wellcome.org/reports/improving-sustainability-vaccine-innovation-ecosystem-africa

25. Ndomondo-Sigonda M, Miot J, Naidoo S, et al. Harmonization of medical products regulation: a key factor for improving regulatory capacity in the East African Community. *BMC Public Health*. 2021;21(1):187. doi:10.1186/s12889-021-10169-1

26. O'Brien J, Lumsden R, Macdonald J. Strengthening regulatory systems for medicines in a changed world: where do we go from here? *BMJ Glob Health*. 2021;6(1):e004680. doi:10.1136/bmjgh-2020-004680

27. Klein K, Stolk P, Tellner P, Acha V, Montagne S, Stöckert I. Regulatory Flexibilities and Guidances for Addressing the Challenges of COVID-19 in the EU: What Can We Learn from Company Experiences? *Ther Innov Regul Sci*. 2022;56(2):366-377. doi:10.1007/s43441-022-00383-3

28. Bolislis WR, de Lucia ML, Dolz F, et al. Regulatory Agilities in the Time of COVID-19: Overview, Trends, and Opportunities. *Clin Ther*. 2021;43(1):124-139. doi:10.1016/j.clinthera.2020.11.015

29. Making the Case: How Regulatory Harmonisation Can Save Lives. Accessed March 13, 2024. https://www.path.org/our-impact/resources/making-case-how-regulatory-harmonisation-can-save-lives-africa/

30. Getting Quality Medicines to Patients Faster in Africa: How to Solve Access Issues - IQVIA. Accessed March 12, 2024. https://www.iqvia.com/locations/middle-east-and-africa/blogs/2023/01/getting-quality-medicines-to-patients-faster-in-africa-how-to-solve-for-access-issues

31. Moeti L, Litedu M, Joubert J. Regulatory registration timelines of generic medicines in South Africa: Assessment of the performance of SAHPRA between 2011 and 2022. *J Pharm Policy Pract*. 2023;16(1):34. doi:10.1186/s40545-023-00537-0

32. Sithole T, Mahlangu G, Capote V, et al. Evaluation of the Review Models and Approval Timelines of Countries Participating in the Southern African Development Community: Alignment and Strategies for Moving Forward. *Front Med*. 2021;8:742200. doi:10.3389/fmed.2021.742200

33. Williams J. CIRS RD Briefing 71 – Trends in the regulatory landscape Latin America – CIRS. Accessed April 5, 2024. https://www.cirsci.org/publications/cirs-rd-briefing-71-trends-in-the-regulatory-landscape-latin-america/

34. Williams J. CIRS RD Briefing 72 – Trends in the regulatory landscape Asia – CIRS. Accessed April 4, 2024. https://www.cirsci.org/publications/cirs-rd-briefing-72-trends-in-the-regulatory-landscape-asia/

35. Sharpe J. CIRS RD Briefing 58: Changing regulatory environment in Latin America – CIRS. Accessed April 5, 2024. https://www.cirsci.org/publications/cirs-rd-briefing-58-changing-regulatory-environment-in-latin-america/

36. Simpson S, Chakrabarti A, Robinson D, Chirgwin K, Lumpkin M. Navigating facilitated regulatory pathways during a disease X pandemic. *Npj Vaccines*. 2020;5(1):1-9. doi:10.1038/s41541-020-00249-5

37. Rawson NSB. Canadian, European and United States new drug approval times now relatively similar. *Regul Toxicol Pharmacol*. 2018;96:121-126. doi:10.1016/j.yrtph.2018.05.002

38. 1 in 10 medical products in developing countries is substandard or falsified | Infectious Diseases Data Observatory. Accessed March 12, 2024. https://www.iddo.org/news/1-10-medical-products-developing-countries-substandard-or-falsified

39. List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3) and maturity level 4 (ML4). Accessed March 17, 2024. https://www.who.int/publications/m/item/list-of-nras-operating-at-ml3-and-ml4

40. Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade (second edition). Accessed March 12, 2024. https://www.wto.org/english/res_e/publications_e/who-wipo-wto_2020_e.htm

41. How Tariffs Impact Access to Medicines. Geneva Network. Published October 12, 2021. Accessed March 12, 2024. https://geneva-network.com/research/how-tariffs-impact-access-to-medicines/

42. Export restrictions do not help fight COVID-19 | UNCTAD. Published June 11, 2021. Accessed April 5, 2024. https://unctad.org/news/export-restrictions-do-not-help-fight-covid-19

43. Velásquez G. Rethinking Global and Local Manufacturing of Medical Products After COVID-19. In: Velásquez G, ed. *Vaccines, Medicines and COVID-19: How Can WHO Be Given a Stronger Voice*?. SpringerBriefs in Public Health. Springer International Publishing; 2022:39-58. doi:10.1007/978-3-030-89125-1_3

44. Export Restrictions in Response to the COVID-19 Pandemic. Accessed April 5, 2024. https://www.everycrsreport.com/reports/IF11551.html

45. Casey CA, Cimino-Isaacs CD. Export Restrictions in Response to the COVID-19 Pandemic.

46. Banik N, Stevens P. Pharmaceutical tariffs, trade flows and emerging economies. Published online 2015.

47. Prosser W, Spisak C, Hatch B, McCord J, Tien M, Roche G. Designing supply chains to meet the growing need of vaccines: evidence from four countries. *J Pharm Policy Pract*. 2021;14(1):80. doi:10.1186/s40545-021-00368-x

48. Making medical-devices supply chains more resilient | McKinsey. Accessed March 12, 2024. https://www.mckinsey.com/capabilities/operations/our-insights/the-resilience-imperative-for-medtech-supply-chains

49. Pisa M. Improving Global Health Supply Chains through Traceability.

50. Jbaily A, Feldhaus I, Bigelow B, et al. Toward health system strengthening in low- and middle-income countries: insights from mathematical modeling of drug supply chains. *BMC Health Serv Res*. 2020;20(1):776. doi:10.1186/s12913-020-05549-z

51. Moyazzem Hossain Md, Abdulla F, Rahman A. Challenges and difficulties faced in low- and middle-income countries during COVID-19. *Health Policy OPEN*. 2022;3:100082. doi:10.1016/j.hpopen.2022.100082

52. Rahmani K, Karimi S, Rezayatmand R, Raeisi AR. Value-Based procurement for medical devices: A scoping review. *Med J Islam Repub Iran*. 2021;35:134. doi:10.47176/mjiri.35.134

53. Babigumira JB, Jenny AM, Bartlein R, Stergachis A, Garrison LP. Health technology assessment in low- and middle-income countries: a landscape assessment. *J Pharm Health Serv Res*. 2016;7(1):37-42. doi:10.1111/jphs.12120

54. CRA interviews with Health Technology Developer representatives.

55. Global spending on health: Weathering the storm. Accessed April 25, 2024. https://www.who.int/publications-detail-redirect/9789240017788

56. Out-of-pocket payments for primary health care unaffordable for millions in Europe, new WHO report shows. Accessed April 6, 2024. https://www.who.int/europe/news/item/12-12-2023-out-of-pocket-payments-for-primary-health-care-unaffordable-for-millions-in-europe-new-who-report-shows

57. Bolongaita S, Lee Y, Johansson KA, et al. Financial hardship associated with catastrophic out-of-pocket spending tied to primary care services in low- and lower-middle-income countries: findings from a modeling study. *BMC Med*. 2023;21(1):356. doi:10.1186/s12916-023-02957-w

58. Adebisi YA, Nwogu IB, Alaran AJ, et al. Revisiting the issue of access to medicines in Africa: Challenges and recommendations. *Public Health Chall*. 2022;1(2):e9. doi:10.1002/puh2.9

59. Key issues for health workforce in the Global Monitoring Report 2023. Accessed March 13, 2024. https://www.who.int/publications/m/item/2023_hwf_gmr

60. Olayemi E, Asare EV, Benneh-Akwasi Kuma AA. Guidelines in lower-middle income countries. *Br J Haematol*. 2017;177(6):846-854. doi:10.1111/bjh.14583

61. Dawkins B, Renwick C, Ensor T, Shinkins B, Jayne D, Meads D. What factors affect patients' ability to access healthcare? An overview of systematic reviews. *Trop Med Int Health*. 2021;26(10):1177-1188. doi:10.1111/tmi.13651

62. Hatzenbuehler ML, Phelan JC, Link BG. Stigma as a fundamental cause of population health inequalities. *Am J Public Health*. 2013;103(5):813-821. doi:10.2105/AJPH.2012.301069

63. Wiysonge CS, Ndwandwe D, Ryan J, et al. Vaccine hesitancy in the era of COVID-19: could lessons from the past help in divining the future? *Hum Vaccines Immunother*. 18(1):1-3. doi:10.1080/21645515.2021.1893062

64. Sen-Crowe B, Sutherland M, McKenney M, Elkbuli A. A Closer Look Into Global Hospital Beds Capacity and Resource Shortages During the COVID-19 Pandemic. *J Surg Res*. 2021;260:56-63. doi:10.1016/j.jss.2020.11.062

65. Cerf ME. Quintile distribution of health resourcing in Africa. Gao Y, ed. *Cogent Med*. 2021;8(1):1997161. doi:10.1080/2331205X.2021.1997161

66. Ahmat A, Asamani JA, Illou MMA, et al. Estimating the threshold of health workforce densities towards universal health coverage in Africa. *BMJ Glob Health*. 2022;7(Suppl 1):e008310. doi:10.1136/bmjgh-2021-008310

67. de Oliveira DR, Griep RH, Portela LF, Rotenberg L. Intention to leave profession, psychosocial environment and self-rated health among registered nurses from large hospitals in Brazil: a cross-sectional study. *BMC Health Serv Res*. 2017;17(1):21. doi:10.1186/s12913-016-1949-6

68. Wagstaff A, Flores G, Smitz MF, Hsu J, Chepynoga K, Eozenou P. Progress on impoverishing health spending in 122 countries: a retrospective observational study. *Lancet Glob Health*. 2018;6(2):e180-e192. doi:10.1016/S2214-109X(17)30486-2

69. World Bank Open Data. World Bank Open Data. Accessed March 12, 2024. https://data.worldbank.org

70. Asante A, Wasike WSK, Ataguba JE. Health Financing in Sub-Saharan Africa: From Analytical Frameworks to Empirical Evaluation. *Appl Health Econ Health Policy*. 2020;18(6):743-746. doi:10.1007/s40258-020-00618-0

71. OECD, Organization WH. *Financing of Health Care from Households' out-of-Pocket Payments and Voluntary Payment Schemes*. OECD; 2022. doi:10.1787/f9c4c084-en

72. OECD, The World Bank. *Health at a Glance: Latin America and the Caribbean 2020*. OECD; 2020. doi:10.1787/6089164f-en

73. Abiye Z, Tesfaye A, Hawaze S. Barriers to access: availability and affordability of essential drugs in a retail outlet of a public health center in south western Ethiopia. *J Appl Pharm Sci*. 2013;3,(10):101-105. doi:10.7324/JAPS.2013.31017

74. Boniol M, Kunjumen T, Nair TS, Siyam A, Campbell J, Diallo K. The global health workforce stock and distribution in 2020 and 2030: a threat to equity and "universal" health coverage? *BMJ Glob Health*. 2022;7(6):e009316. doi:10.1136/bmjgh-2022-009316

75. The Moment of Truth for Healthcare Spending: How Payment Models can Transform Healthcare Systems. World Economic Forum. Accessed September 18, 2023. https://www.weforum.org/reports/the-moment-of-truth-for-healthcare-spending-how-payment-models-can-transform-healthcare-systems/

76. Directorate-General for Health and Food Safety (European Commission), Ecorys BV, Milieu Law & Policy Consulting, et al. *Future-Proofing Pharmaceutical Legislation: Study on Medicine Shortages : Final Report*. Publications Office of the European Union; 2021. Accessed May 20, 2024. https://data.europa.eu/doi/10.2875/211485

77. Partnerships for African Vaccine Manufacturing (PAVM) Framework for Action. Africa CDC. Accessed March 13, 2024. https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/

78. African Vaccine Manufacturing Accelerator (AVMA). Accessed June 25, 2024. https://www.gavi.org/programmes-impact/types-support/regional-manufacturing-strategy/avma

79. Launch of the Regional Platform to Advance the Manufacturing of COVID-19 Vaccines and other Health Technologies in the Americas - PAHO/WHO | Pan American Health Organization. Accessed March 13, 2024. https://www.paho.org/en/events/launch-regional-platform-advance-manufacturing-covid-19-vaccines-and-other-health

80. Singapore's Advanced Manufacturing Will Attract Greater Pharmaceutical Investments. Fitch Solutions. Published September 5, 2022. Accessed March 15, 2024. https://www.fitchsolutions.com/bmi/pharmaceuticals/singapores-advanced-manufacturing-will-attract-greater-pharmaceutical-investments-05-09-2022

81. Pearce F, Lin L, Teo E, Ng K, Khoo D. Health Technology Assessment and Its Use in Drug Policies: Singapore. *Value Health Reg Issues*. 2019;18:176-183. doi:10.1016/j.vhri.2018.03.007

82. COVID-19 Vaccines with WHO Emergency Use Listing | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Accessed May 15, 2024. https://extranet.who.int/prequal/vaccines/covid-19-vaccines-who-emergency-use-listing

83. Health dept defends Cipla after Biovac claims unfair tender award. Accessed March 13, 2024. https://www.dailymaverick.co.za/article/2023-04-20-health-department-comes-to-ciplas-defence-after-biovac-claim-tender-was-unfair/

84. Indian Pharma: A Global Leader Under Pressure. Institut Montaigne. Accessed April 6, 2024. https://www.institutmontaigne.org/en/expressions/indian-pharma-global-leader-under-pressure

85. India IB. Indian Policies to Promote Local Production of Pharmaceutical Products and Protect Public Health. Indian Policies to Promote Local Production of Pharmaceutical Products and Protect Public Health. Accessed April 6, 2024. https://www.ganeshremedies.com/advanced-intermediates-environment-care

86. Lahariya C. A brief history of vaccines & vaccination in India. *Indian J Med Res*. 2014;139(4):491-511.

87. Insights From India on Expanding Global Vaccine Production | Think Global Health. Council on Foreign Relations. Accessed April 6, 2024. https://www.thinkglobalhealth.org/article/insights-india-expanding-global-vaccine-production

88. Sarda S. Will India's pharma sector be able to come out of its China dependence? The Economic Times. https://economictimes.indiatimes.com/industry/healthcare/biotech/pharmaceuticals/will-indias-pharma-sector-be-able-to-come-out-of-its-china-dependence/articleshow/108048363.cms?from=mdr. Published February 27, 2024. Accessed April 25, 2024.

89. Africa CDC warns COVID-19 vaccine production could cease - PMC. Accessed March 13, 2024. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9049880/

90. Statement on Kenya Manufacturing Facility. Accessed April 25, 2024. https://investors.modernatx.com/Statements--Perspectives/Statements--Perspectives-Details/2024/Statement-on-Kenya-Manufacturing-Facility/default.aspx

91. Salam U, Lee S, Fullerton V, Yusuf Y, Krantz S, Henstridge M. Indonesia case study: Rapid technological change – challenges and opportunities. *Pathw Prosper Comm Backgr Pap Ser*. 2018;(8):1-72.

92. Local content regulation for pharma not the panacea - Opinion - The Jakarta Post. Accessed March 15, 2024. https://www.thejakartapost.com/academia/2020/06/17/local-content-regulation-for-pharma-not-the-panacea.html

93. Fanda RB, Probandari A, Yuniar Y, et al. The availability of essential medicines in primary health centres in Indonesia: achievements and challenges across the archipelago. *Lancet Reg Health - Southeast Asia*. 2024;0(0). doi:10.1016/j.lansea.2023.100345

94. Stone S, Messent J, Flaig D. *Emerging Policy Issues: Localisation Barriers to Trade*. OECD; 2015. doi:10.1787/5js1m6v5qd5j-en

95. Post-COVID Supply Chains: Lockdown Lessons Learned. PharmTech. Published June 9, 2023. Accessed April 26, 2024. https://www.pharmtech.com/view/post-covid-supply-chains-lockdown-lessons-learned

96. Is localisation the answer for pharmaceutical supply chain resilience? *Eur Pharm Rev*. Accessed April 26, 2024. https://www.europeanpharmaceuticalreview.com/article/174401/is-localisation-the-answer-for-pharmaceutical-supply-chain-resilience/

97. COVID-19: How companies are changing track to join the fight. World Economic Forum. Published March 24, 2020. Accessed May 15, 2024. https://www.weforum.org/agenda/2020/03/from-perfume-to-hand-sanitiser-tvs-to-face-masks-how-companies-are-changing-track-to-fight-covid-19/

98. Mukherjee S, Kalra K, Phelan AL. Expanding global vaccine manufacturing capacity: Strategic prioritization in small countries. *PLOS Glob Public Health*. 2023;3(6):e0002098. doi:10.1371/journal.pgph.0002098

99. Massuda A, Hone T, Leles FAG, Castro MC de, Atun R. The Brazilian health system at crossroads: progress, crisis and resilience. *BMJ Glob Health*. 2018;3(4):e000829. doi:10.1136/bmjgh-2018-000829

100. Coube M, Nikoloski Z, Mrejen M, Mossialos E. Inequalities in unmet need for health care services and medications in Brazil: a decomposition analysis. *Lancet Reg Health – Am*. 2023;19. doi:10.1016/j.lana.2022.100426

101. A Polio-Free India Is One of the Biggest Achievements in Global Health. World Bank. Accessed March 13, 2024. https://www.worldbank.org/en/news/feature/2014/05/29/polio-free-india-biggest-achievements-global-health

102. Healthy Markets for Health Investments: Policy Considerations from the Private Sector. Published December 6, 2022. Accessed March 14, 2024. https://www.uschamber.com/international/healthy-markets-for-health-investments-policy-considerations-from-the-private-sector

103. 2023 International IP Index. Published February 21, 2023. Accessed March 12, 2024. https://www.uschamber.com/intellectual-property/2023-international-ip-index

104. Zainol ZA, Amin L, Jusoff K, Zahid A, Akpoviri F. Pharmaceutical patents and access to essential medicines in sub-Saharan Africa. *Afr J Biotechnol*. 2011;10(58):12376-12388.

105. Velásquez G. Intellectual Property and Access to Medicines and Vaccines. In: Velásquez G, ed. *Vaccines, Medicines and COVID-19: How Can WHO Be Given a Stronger Voice?*. SpringerBriefs in Public Health. Springer International Publishing; 2022:73-92. doi:10.1007/978-3-030-89125-1_5

106. Motari M, Nikiema JB, Kasilo OMJ, et al. The role of intellectual property rights on access to medicines in the WHO African region: 25 years after the TRIPS agreement. *BMC Public Health*. 2021;21(1):490. doi:10.1186/s12889-021-10374-y

107. Stevens H, Huys I. Innovative Approaches to Increase Access to Medicines in Developing Countries. Front Med. 2017;4. Accessed December 6, 2023. https://www.frontiersin.org/articles/10.3389/fmed.2017.00218

108. Mermelstein S, Stevens H. TRIPS to Where? A Narrative Review of the Empirical Literature on Intellectual Property Licensing Models to Promote Global Diffusion of Essential Medicines. *Pharmaceutics*. 2021;14(1):48. doi:10.3390/pharmaceutics14010048

109. Popzyk G. Export Controls and Export Bans over the Course of the Covid-19 Pandemic. *Fed Ger Ind BDI*. Published online 2020. https://www.wto.org/english/tratop_e/covid19_e/bdi_covid19_e.pdf

110. Anyangwe SCE, Mtonga C. Inequities in the Global Health Workforce: The Greatest Impediment to Health in Sub-Saharan Africa. *Int J Environ Res Public Health*. 2007;4(2):93-100. doi:10.3390/ijerph2007040002

111. Chronic staff shortfalls stifle Africa's health systems: WHO study. WHO | Regional Office for Africa. Published March 10, 2024. Accessed March 12, 2024. https://www.afro.who.int/news/chronic-staff-shortfalls-stifle-africas-health-systems-who-study

112. WHO guideline on country pharmaceutical pricing policies. Accessed October 25, 2022. https://www.who.int/publications-detail-redirect/9789240011878

113. Winberg DR, Lu Y, Chen Y, Shi L. Can health technology assessments assist the global campaign against poverty? *Glob Health J*. 2021;5(3):116-119. doi:10.1016/j.glohj.2021.07.005

114. Ensuring access to medicines: how to redesign pricing, reimbursement and procurement? Accessed March 14, 2024. https://eurohealthobservatory.who.int/publications/i/ensuring-access-to-medicines-how-to-redesign-pricing-reimbursement-and-procurement

115. Koduah A, Baatiema L, de Chavez AC, et al. Implementation of medicines pricing policies in sub-Saharan Africa: systematic review. *Syst Rev*. 2022;11(1):257. doi:10.1186/s13643-022-02114-z

116. Kredo T, Bernhardsson S, Machingaidze S, et al. Guide to clinical practice guidelines: the current state of play. *Int J Qual Health Care*. 2016;28(1):122-128. doi:10.1093/intqhc/mzv115

117. Improving Access to Medicines in Low and Middle Income Countries: Corporate Responsibilities in Context - PMC. Accessed March 12, 2024. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3606933/

118. Reducing health inequalities and improving access to medicine through access and affordability programmes - Thoughts from the Centre | Deloitte UK. Accessed March 12, 2024. https://blogs.deloitte.co.uk/health/2021/12/reducing-health-inequalities-and-improving-access-to-medicine-through-access-and-affordability-progr.html

119. Luiza VL, Mendes LVP, Tavares NUL, et al. Inappropriate use of medicines and associated factors in Brazil: an approach from a national household survey. *Health Policy Plan*. 2019;34(Supplement_3):iii27-iii35. doi:10.1093/heapol/czz038

120. Investment in expanding clinics and hospitals improving Algeria's health indicators - Africa 2015 - Oxford Business Group. Published January 20, 2016. Accessed March 12, 2024. https://oxfordbusinessgroup.com/reports/algeria/2015-report/economy/a-focal-point-investing-in-improving-infrastructure-and-facilitating-growth-in-a-local-pharmaceuticals-industry

121. Laouisset DE. Algeria import substitution policy: the case of the pharmaceutical industry. *Cah Cread*. 2021;37(1):5-39.

122. Algeria's Medicine Supply Shortage: Local Measures for a Global Problem. PharmaBoardroom. Accessed March 12, 2024. https://pharmaboardroom.com/articles/algerias-medicine-supply-shortage-local-measures-for-a-global-problem/

123. Dahmani H, Fradi I, Achour L, Toumi M, Maghreb Research Group. Pharmaceutical pricing and reimbursement policies in Algeria, Morocco, and Tunisia: comparative analysis. *J Mark Access Health Policy*. 2023;11(1):2244304. doi:10.1080/20016689.2023.2244304

124. Global Access to New Medicines Report.

125. لي اب اش ف, كواش ز. الرعاية الصحية العواقب و الأدوية بين الطفولة و الأمومة و آفاق آفاق. 2023;11(3):55-77.

126. Algeria's new 2020 Finance Act | DLA Piper Africa, Algeria | L&P Partners. DLA Piper Africa. Published January 1, 2020. Accessed March 15, 2024. https://www.dlapiperafrica.com/en/algeria/insights/2020/legal-update-algerias-2020-finance-act.html

127. Self-Sufficiency Initiatives Will Reduce Pharmaceutical Imports And Limit Opportunities For Multinational Firms In Algeria. Fitch Solutions. Published October 18, 2022. Accessed March 15, 2024. https://www.fitchsolutions.com/bmi/pharmaceuticals/self-sufficiency-initiatives-will-reduce-pharmaceutical-imports-and-limit-opportunities-multinational-firms-algeria-18-10-2022

128. Algerian pharmaceutical boom paves way to health security. euronews. Published September 19, 2022. Accessed March 15, 2024. https://www.euronews.com/2022/09/19/algerian-pharmaceutical-boom-a-step-towards-health-food-security

129. Country Report: Algeria. Published online December 1, 2014. Accessed March 15, 2024. https://www.pharmexec.com/view/country-report-algeria

130. SciELO - Brazil - Barriers to access to medicines for non-communicable diseases for patients using the Brazilian Unified Health System (SUS) Barriers to access to medicines for non-communicable diseases for patients using the Brazilian Unified Health System (SUS). Accessed March 12, 2024. https://www.scielo.br/j/bjps/a/fMLzRYmGHZRxGKKRRyQZytk/?lang=en

131. Effect of socioeconomic inequalities and vulnerabilities on health-system preparedness and response to COVID-19 in Brazil: a comprehensive analysis - The Lancet Global Health. Accessed March 12, 2024. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00081-4/fulltext

132. Interpat. Accessed March 15, 2024. https://www.interpat.org/resources/brazil-ip-study-updated/

133. Current health expenditure (% of GDP) | Data. Accessed March 12, 2024. https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS

134. Health equipment - Hospital beds - OECD Data. theOECD. Accessed March 15, 2024. http://data.oecd.org/healtheqt/hospital-beds.htm

135. OECD. *OECD Reviews of Health Systems: Brazil 2021*. OECD; 2021. doi:10.1787/146d0dea-en

136. Apolinario D, Mansur LL, Carthery-Goulart MT, Brucki SMD, Nitrini R. Detecting limited health literacy in Brazil: development of a multidimensional screening tool. *Health Promot Int*. 2014; 29(1):5-14. doi:10.1093/heapro/dat074

137. Naves J de OS, Silver LD. [Evaluation of pharmaceutical assistance in public primary care in Brasilia, Brazil]. *Rev Saude Publica*. 2005;39(2):223-230. doi:10.1590/s0034-89102005000200013

138. Legislative Assembly of the State of Rio de Janeiro. Accessed March 15, 2024. https://www.alerj.rj.gov.br/Visualizar/

139. Perfil da Indústria Farmacêutica e Aspectos Relevantes do Setor. Accessed March 15, 2024. https://sindusfarma.org.br/publicacoes/exibir/20651-perfil-da-industria-farmaceutica-e-aspectos-relevantes-do-setor

140. SciELO - Brazil - Brazilian national production of active pharmaceutical ingredients: regulatory and strategic framework Brazilian national production of active pharmaceutical ingredients: regulatory and strategic framework. Accessed March 15, 2024. https://www.scielo.br/j/aabc/a/PkFRyxPj83bs78QhzmZ3ZXy/?lang=en

141. NHM :: National Health Mission. Accessed March 12, 2024. https://nhm.gov.in/index4.php?lang=1&level=0&linkid=445&lid=38

142. Hannah E, Basheer N, Dumka N, Kotwal A. Access to medicines in the Indian Public Health System – what works and what does not? A review of the National Health Mission Common Review Mission Reports (2007-2021). *J Glob Health Rep*. 2023;7:e2023054. doi:10.29392/001c.84486

143. Tripathi N, Kerketta F, Chatterjee P, Raman VR, John D, Jain K. Access and availability of essential medicines in Chhattisgarh: Situation in public health facilities. *J Fam Med Prim Care*. 2018;7(1):152. doi:10.4103/jfmpc.jfmpc_78_17

144. Regulatory Challenges of Indian Drugs. Accessed March 12, 2024. https://www.drishtiias.com/daily-updates/daily-news-editorials/regulatory-challenges-of-indian-drugs

145. 6% of medicine samples picked up in November are substandard | India News - Times of India. Accessed March 12, 2024. https://timesofindia.indiatimes.com/india/6-of-medicine-samples-picked-up-in-november-are-substandard/articleshow/96632600.cms?from=mdr

146. Medicines in India: Accessibility, affordability and quality. Brookings. Accessed March 15, 2024. https://www.brookings.edu/articles/medicines-in-india-accessibility-affordability-and-quality/

147. National Regulatory Authority of India meets WHO international standards for vaccine regulations. Accessed March 12, 2024. https://www.who.int/india/news/detail/12-07-2017-national-regulatory-authority-of-india-meets-who-international-standards-for-vaccine-regulations

148. Mcintyre D, Meheus F, Røttingen JA. What level of domestic government health expenditure should we aspire to for universal health coverage? *Health Econ Policy Law*. 2017;12(2):125-137. doi:10.1017/S1744133116000414

149. Hospital beds and discharges | Health at a Glance: Europe 2022 : State of Health in the EU Cycle | OECD iLibrary. Accessed March 12, 2024. https://www.oecd-ilibrary.org/sites/518727bb-en/index.html?itemId=/content/component/518727bb-en

150. Kasthuri A. Challenges to Healthcare in India - The Five A's. *Indian J Community Med Off Publ Indian Assoc Prev Soc Med*. 2018;43(3):141-143. doi:10.4103/ijcm.IJCM_194_18

151. Global Health Workforce statistics database. Accessed March 12, 2024. https://www.who.int/data/gho/data/themes/topics/health-workforce

152. Sharma DC. India still struggles with rural doctor shortages. *The Lancet*. 2015;386(10011):2381-2382. doi:10.1016/S0140-6736(15)01231-3

153. From Insights to Impact: Building confidence in routine childhood vaccines in India | UNICEF. Accessed March 15, 2024. https://www.unicef.org/documents/insights-impact-building-confidence-routine-childhood-vaccines-india

154. Tracking Universal Health Coverage: 2023 Global monitoring report. Accessed March 15, 2024. https://www.who.int/publications-detail-redirect/9789240080379

155. Out-of-pocket expenditure as percentage of current health expenditure (CHE) (%). Accessed March 12, 2024. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/out-of-pocket-expenditure-as-percentage-of-current-health-expenditure-(che)-(-)

156. Population pushed below the $3.20 a day poverty line by household health expenditures (%, national, rural, urban). Accessed March 12, 2024. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/population-pushed-below-the-3.20-a-day-poverty-line-by-household-health-expenditures

157. Make in India: Country emerges as the new hub of vaccine research. Hindustan Times. Published October 16, 2017. Accessed March 15, 2024. https://www.hindustantimes.com/india-news/make-in-india-country-emerges-the-new-hub-of-vaccine-research/story-ireKtJcZCBjSdsuDaO4k9O.html

158. Scaling up African vaccine manufacturing capacity | Reports. Wellcome. Published January 25, 2023. Accessed December 6, 2023. https://wellcome.org/reports/scaling-african-vaccine-manufacturing-capacity

159. PHARMACEUTICALS EXPORT PROMOTION COUNCIL OF INDIA. Accessed March 15, 2024. https://pharmexcil.com/

160. Biotechnology Industry Research Assistance Council (BIRAC) — Vikaspedia. Accessed March 15, 2024. https://vikaspedia.in/education/resource-links/scientific-and-educational-institutions/biotechnology-industry-research-assistance-council-birac

161. Swarup R, Sharma A, Logani JM. Building a robust ecosystem for vaccine research in India. *Int J Infect Dis*. 2019;84:S7-S9. doi:10.1016/j.ijid.2019.03.017

162. Notification of Electronic Products under the Public Procurement (Preference to Make in India) Order 2017 | Ministry of Electronics and Information Technology, Government of India. Accessed May 16, 2024. https://www.meity.gov.in/esdm/ppo

163. Prequalified Vaccines | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control). Accessed March 15, 2024. https://extranet.who.int/prequal/vaccines/prequalified-vaccines

164. How much vaccines can India make? And the catch... Business Today. Published April 13, 2021. Accessed March 15, 2024. https://www.businesstoday.in/coronavirus/story/after-launching-how-much-vaccine-can-india-make-and-the-catch-293353-2021-04-13

165. Indian vaccine makers gaining wider market share in industry. *The Economic Times*. https://economictimes.indiatimes.com/news/india/indian-vaccine-makers-gaining-wider-market-share-in-industry/articleshow/93769720.cms. Published August 25, 2022. Accessed March 15, 2024.

166. Universal Immunization Programme (UIP) | Ministry of Health and Family Welfare | GOI. Accessed March 15, 2024. https://main.mohfw.gov.in/?q=Major-Programmes/universal-immunization-programme-uip

167. INDIA: A push to vaccinate every child, everywhere, ended polio in India. Accessed March 15, 2024. https://www.who.int/india/news/feature-stories/detail/a-push-to-vaccinate-every-child-everywhere-ended-polio-in-india

168. Health cess is discriminatory since it is imposed on a specific sector, and on import of specific devices - Opinion News | The Financial Express. Accessed March 12, 2024. https://www.financialexpress.com/opinion/health-cess-is-discriminatory-since-it-is-imposed-on-a-specific-sector-and-on-import-of-specific-devices/1879367/

169. Research Reports - Public Health Foundation of India. Published November 28, 2016. Accessed March 15, 2024. https://phfi.org/research-reports/

170. India's Serum Institute applies for full approval of Covishield vaccine. *Reuters*. https://www.reuters.com/world/india/indias-serum-institute-applies-full-approval-covishield-vaccine-2021-12-31/. Published December 31, 2021. Accessed March 15, 2024.

171. The Capacity of the Indonesian Healthcare System to Respond to COVID-19 - PMC. Accessed March 12, 2024. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8292619/

172. Urban and Rural Disparities in Hospital Utilization among Indonesian Adults - PubMed. Accessed March 12, 2024. https://pubmed.ncbi.nlm.nih.gov/31205878/

173. Agustina R, Dartanto T, Sitompul R, et al. Universal health coverage in Indonesia: concept, progress, and challenges. *The Lancet*. 2019;393(10166):75-102. doi:10.1016/S0140-6736(18)31647-7

174. Mendorong Investasi Asing Langsung Di Sektor Farmasi. Accessed March 15, 2024. https://web.indef.or.id/research/detail/mendorong-investasi-asing-langsung-di-sektor-farmasi

175. MOH | Achieving more with less - Singapore's healthcare expenditure. Accessed March 12, 2024. https://www.moh.gov.sg/resources-statistics/educational-resources/achieving-more-with-less---singapore's-healthcare-expenditure

176. Tan CC, Lam CSP, Matchar DB, Zee YK, Wong JEL. Singapore's health-care system: key features, challenges, and shifts. *The Lancet*. 2021;398(10305):1091-1104. doi:10.1016/S0140-6736(21)00252-X

177. Lymphoma Coalition Asia Pacific – Lymphoma Coalition. Accessed March 15, 2024. https://lymphomacoalition.org/asia-pacific/

178. Process & Methods. ACE. Accessed March 12, 2024. https://www.ace-hta.gov.sg/resources/process-methods

179. 10-point plan to improve health system in SA | SAnews. Accessed March 12, 2024. https://www.sanews.gov.za/south-africa/10-point-plan-improve-health-system-sa

180. Schaay N, Sanders D, Kruger V. OVERVIEW OF HEALTH SECTOR REFORMS IN SOUTH AFRICA. Published online 2011.

181. The Compounding Effect of Tariffs on Medicines: Estimating the Real Cost of Emerging Markets' Protectionism |. Accessed March 15, 2024. https://ecipe.org/publications/the-compounding-effect-of-tariffs-on-medicines-estimating-the-real-cost-of-emerging-markets-protectionism/

182. Haakenstad A, Irvine CMS, Knight M, et al. Measuring the availability of human resources for health and its relationship to universal health coverage for 204 countries and territories from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2022;399(10341):2129-2154. doi:10.1016/S0140-6736(22)00532-3

183. Zuma S. CHALLENGES ASSOCIATED WITH PROVISION OF ESSENTIAL MEDICINES IN THE REPUBLIC OF SOUTH AFRICA AND OTHER SELECTED AFRICAN COUNTRIES. *World J Pharm Res*. Published online August 3, 2019. doi:10.20959/wjpr20199-15303

184. Magadzire BP, Ward K, Leng HMJ, Sanders D. Inefficient procurement processes undermine access to medicines in the Western Cape Province of South Africa. *S Afr Med J*. 2017;107(7):581-584. doi:10.7196/SAMJ.2017.v107i7.11356

185. Modisakeng C, Matlala M, Godman B, Meyer JC. Medicine shortages and challenges with the procurement process among public sector hospitals in South Africa; findings and implications. *BMC Health Serv Res*. 2020;20(1):234. doi:10.1186/s12913-020-05080-1

186. Zuma S. Medicine stockouts are a problem in South Africa's clinics: how pharmacist assistants can help. The Conversation. Published March 16, 2023. Accessed March 12, 2024. http://theconversation.com/medicine-stockouts-are-a-problem-in-south-africas-clinics-how-pharmacist-assistants-can-help-198922

187. The state of the health workforce in the WHO African Region - 2021. WHO | Regional Office for Africa. Published March 13, 2024. Accessed March 15, 2024. https://www.afro.who.int/publications/state-health-workforce-who-african-region-2021

188. Vaccine supply and logistics. Accessed March 12, 2024. https://immunizationdata.who.int/pages/indicators-by-category/vaccine_supply.html?ISO_3_CODE=ZAF&YEAR=

189. Assignment Report: Overview of Health Sector Reforms in South Africa | CGIAR GENDER Impact Platform. CGIAR Gender Platform. Accessed March 15, 2024. https://gender.cgiar.org/publications/assignment-report-overview-health-sector-reforms-south-africa

190. Keyter AA. An Evaluation of the Regulatory Environment in South Africa: Improving the Review Process and Patients' Access to Medicines. Published online May 5, 2020. doi:10.18745/th.23022

191. Katerere DR. South Africa needs to tighten controls on substandard and counterfeit medicines. Here's how. The Conversation. Published November 18, 2021. Accessed March 12, 2024. http://theconversation.com/south-africa-needs-to-tighten-controls-on-substandard-and-counterfeit-medicines-heres-how-170233

192. South Africa's vaccine regulator reaches new WHO level to ensure safety, quality and effectiveness. Accessed March 12, 2024. https://www.who.int/news/item/05-10-2022-south-africa-s-vaccine-regulator-reaches-new-who-level-to-ensure-safety-quality-effectiveness

193. Infrastructure Development Act: National Infrastructure Plan 2050 Phase 2: Comments invited | South African Government. Accessed March 15, 2024. https://www.gov.za/documents/notices/infrastructure-development-act-national-infrastructure-plan-2050-phase-2-comments

194. Dell AJ, Kahn D. Geographical maldistribution of surgical resources in South Africa: A review of the number of hospitals, hospital beds and surgical beds. *South Afr Med J Suid-Afr Tydskr Vir Geneeskd*. 2017;107(12):1099-1105. doi:10.7196/SAMJ.2017.v107i12.12539

195. Gumede DM, Taylor M, Kvalsvig JD. Engaging future healthcare professionals for rural health services in South Africa: students, graduates and managers perceptions. *BMC Health Serv Res*. 2021;21(1):220. doi:10.1186/s12913-021-06178-w

196. Total density per 100 000 population: District/rural hospitals. Accessed March 12, 2024. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/total-density-per-100-000-population-district-rural-hospitals

197. The State of the World's Children 2023 | UNICEF. Published April 20, 2023. Accessed March 15, 2024. https://www.unicef.org/reports/state-worlds-children-2023

198. Walwyn DR, Nkolele AT. An evaluation of South Africa's public–private partnership for the localisation of vaccine research, manufacture and distribution. *Health Res Policy Syst*. 2018;16(1):30. doi:10.1186/s12961-018-0303-3

199. Makhoana M. Establishing human vaccine manufacturing in Southern Africa. *Vaccine Technol IV*. Published online May 21, 2012. https://dc.engconfintl.org/vaccine_iv/9

200. Sanofi and Pfizer engage Biovac Institute with vaccines production in South Africa. Accessed March 15, 2024. https://manufacturingchemist.com/news/article_page/Sanofi_and_Pfizer_engage_Biovac_Institute_with_vaccines_production_in_South_Africa/156848

201. Abbott FM, Abbott RB, Fortunak J, Sampath PG, Walwyn D. Opportunities, Constraints and Critical Supports for Achieving Sustainable Local Pharmaceutical Manufacturing in Africa: With a focus on the Role of Finance. *Nova Worldw*. Published online 2021. Accessed March 15, 2024. https://diginole.lib.fsu.edu/islandora/object/fsu%3A771574/

202. COVID-19 Coronavirus vaccine | South African Government. Accessed March 15, 2024. https://www.gov.za/covid-19/vaccine/vaccine

203. Tomlinson C. In-depth: After a rough 17 years, is Biovac finally on track? Spotlight. Published January 28, 2021. Accessed March 13, 2024. https://www.spotlightnsp.co.za/2021/01/28/in-depth-after-a-rough-17-years-is-biovac-finally-on-track/

204. Pharmaceutical Industry: Department of Health & DTI briefing | PMG. Accessed March 15, 2024. https://pmg.org.za/committee-meeting/24697/

205. Veller WJ and M. SA's short-sighted vaccine manufacture and procurement policy compromises Africa's development. Daily Maverick. Published May 1, 2023. Accessed March 15, 2024. https://www.dailymaverick.co.za/article/2023-05-01-sas-short-sighted-vaccine-manufacture-and-procurement-policy-compromises-africas-development/

206. CHAI Go-to-market toolbox for DCVMs – DCVMN. Accessed March 15, 2024. https://dcvmn.org/chai-go-to-market-toolbox-for-dcvms/

207. Roelf W. Pfizer, Sanofi, to boost South African Biovac's vaccine output. *Reuters*. https://www.reuters.com/article/idUSKCN1TX1N3/. Published July 3, 2019. Accessed March 15, 2024.

208. Construction of Biovac ultra-cold storage facility completed | SAnews. Accessed March 15, 2024. https://www.sanews.gov.za/south-africa/construction-biovac-ultra-cold-storage-facility-completed

209. Sampath PG. African vaccines: local manufacturers are struggling to access the market - what must change. The Conversation. Published April 25, 2023. Accessed March 15, 2024. http://theconversation.com/african-vaccines-local-manufacturers-are-struggling-to-access-the-market-what-must-change-204136

210. Ebrahim Z. World's first fully liquid vaccine to be locally manufactured by CT-based Biovac. Life. Accessed March 15, 2024. https://www.news24.com/life/wellness/body/condition-centres/infectious-diseases/news/worlds-first-fully-liquid-vaccine-to-be-locally-manufactured-by-ct-based-biovac-20201119

211. Biovac gets shot in the arm from R9.78bn vaccine contract. Accessed March 15, 2024. https://www.businesslive.co.za/bd/national/health/2019-11-26-biovac-gets-shot-in-the-arm-from-r978bn-vaccine-contract/

212. Pfizer partner Biovac warns of production slump amid low COVID vaccine demand: report | Fierce Pharma. Accessed March 15, 2024. https://www.fiercepharma.com/pharma/another-covid-19-manufacturing-partner-time-pfizers-biovac-warns-production-slump-amid-low

213. The mRNA vaccine technology transfer hub. Accessed March 15, 2024. https://www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub

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and the Economy (GIHE)