

# A Path to Resiliency: Mitigating the Impacts of COVID-19 on Essential Medicines Supply Chains

**Anthony McDonnell, Elizabeth Pisani, Somya Singhvi, Kalipso Chalkidou, and Prashant Yadav**

## Abstract

COVID-19 has put a spotlight on health product supply chains, highlighting the challenges in multiple steps in the global supply chain. This paper seeks to understand the impact of COVID-19 on the supply chain of a subset of essential medicines. It identifies the main categories of blockages in the global supply chain created by COVID-19, then uses data on trade flows, wholesalers, and pharma companies, and from surveys, to track the impact.

There was significant short-term disruption to manufacturing caused by COVID-19. Surveys, pharmacy, and export data indicate that COVID-related disruptions impacted the supply of essential medicines, but this varied greatly by markets and product.

The paper highlights that (1) data-driven approaches should be considered to make supply chains more robust, (2) solutions must account for the political and institutional landscape, (3) price surges benefit the wealthiest, and (4) local solutions are often needed to manage global shocks.

More research is needed, particularly into how to obtain granular data to track supply shocks in real time? How do we increase surge capacity? Is it possible to improve procurement practices through pooled procurement, where applicable? And can pharmaceutical production be diversified, with products produced regionally to limit the risk of disruption?

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## **Executive summary**

The Sustainable Development Goals aim to create a world by 2030 where everyone has “access to safe, effective, quality and affordable essential medicines.” To achieve this goal, manufacturers need to produce essential medicines to meet global needs, and supply chains need to be resilient enough to deliver them, even when the world faces major disruption. This paper aims to stimulate debate about the supply chain for essential medicines in low- and middle-income countries (LMICs), especially in sub-Saharan Africa. It focuses on a subset of 64 products that are not procured by global health donors and are largely funded by LMIC governments themselves. It summarises learning from work undertaken between April and October 2020 by the Center for Global Development together with analysts from a number of other organisations and provides an analytical framework for bringing together data of different types (qualitative and quantitative) and from different sources (wholesaler surveys, trade data, retail data) to investigate whether COVID-19-related shocks affected supplies of essential medicines.

### **Six key findings from the research**

Despite clear indication of disrupted supply from India, the world’s largest exporter of essential medicines, we found very little evidence of a consistent or sustained effect of COVID-19 supply shocks across the markets examined. Among the possible reasons are that the pandemic dented demand more than it affected supply; that our data sources and analyses were inadequate to pick up any real effect; or that the global medicine market is robust to short-lived shocks.

The main results of each strand of the research include:

- A. The pandemic disrupted upstream supply of APIs (active pharmaceutical ingredients) from China and the manufacturing of finished products in India. However, the impact was short lived, and manufacturers recovered very quickly. In March 2020, API imports from China to India were down by 24 percent, manufacturing of finished products in India dropped by 44 percent, and export of generic medicines from India fell by 19 percent in value, all compared with March 2019. By May/June 2020, API imports from China and manufacturing and export of Indian finished products had recovered to pre-pandemic levels, although prices of many APIs rose by up to 30 percent and the exports rebound was seen most strongly in exports to North America.
- B. A survey of 27 medicine wholesalers and distributors in six countries did not find any product being reported in short supply in all countries. Also, it found a lack of consistency between reported stockouts and stock in hand. A survey of one subnational and four national central medical stores found that 50 of the study products were normally stocked by at least one of the countries with national stores (Gambia, Malawi, and Senegal), and 17 of them were reported to be in shortage by at least one country. Central medical stores reported shortages as a regular occurrence, not related to COVID-19.

- C. Estimating supply disruptions by comparing changes in Indian export data showed that there were dramatic shifts in some drugs during the period of interest, but they varied a lot by product. Seven of 17 drugs examined showed price increases and volume falls, 3 more saw both prices and volume rise, 4 price falls and volume rises, and 3 where both price and volume fell. Pharmacy data from Ghana, Nigeria, Kenya, and India also showed large variation by product and as well as by market. Inventory was largely unchanged or increased by up to 100 percent for roughly half the molecules of interest, suggesting lower sales. The other half saw inventory decrease by up to 65 percent.
- D. IQVIA and Maisha Meds attempted to develop models that could flag potential supply disruptions before they reached pharmacies. Both models were constrained by poor quality of data, particularly a lack of information on what products had been in shortage historically. IQVIA's model had a very high false positive rate and Maisha Med's only identified about half the drugs that went into shortage.
- E. Aggregating the data from the multiple sources used in this project, there was a correlation ranging from 0.06 to 0.41. Low correlations may be because different sources use different methodologies and examine different parts of the supply chain. More work is needed to understand the information in these various sources provide, and whether they can be combined to give a more comprehensive understanding of the risk of shortages.
- F. Countries in sub-Saharan Africa import most of their medicines. Reducing this dependence on imports by increasing production of solid formulations of essential medicines in sub-Saharan Africa was deemed feasible over time, using a spoke-and-hub model, with initial hubs sited in a handful of areas with good existing infrastructure and transport links. The success of this model depends on high levels of collaboration around trade and medicine regulation.

## **Four lessons from the research**

1. **Data-driven approaches to guarding against the effect of supply shocks are worthy of consideration by national governments as well as the global health organisations that seek to support them.** These efforts will only be effective if there is better use of immediately available data at the country level and more transparency at the global and national level. Our team had access to some of the richest proprietary data about international pharmaceutical markets and we were still unable to trace products through the global supply—from API production in China, through manufacturing of finished products in India, shipment to wholesalers and central medical stores in lower-income countries, and ultimately, retail sale.
2. **Technocratic solutions to supply chain threats are unlikely to work unless they also take into account the political and institutional landscape.** A lot of the discussions about supply chains have focused on the raw market forces of supply and

demand and the technical aspects of production, procurement, and supply planning. However, we find that many of the threats to sustained supply in a globalised supply chain are political.

3. **Profit-seeking, including surge pricing and speculation, cascade through the supply chain, ultimately benefiting buyers who are least price sensitive.** Where many buyers are competing for the same products, shipments to the highest payer may increase, at the expense of patients in lower-income settings. As more countries progress through the epidemiological transition and are increasingly affected by non-communicable diseases, this competition for similar products is likely to grow. Countries which focus largely on achieving the lowest prices for quality-assured products in public procurement put themselves at risk of being outbid in times of shortage. At the very least, flexibilities must be built into procurement law to allow for rapid response in times of crisis.
4. **Local solutions are often needed to manage global shocks** A few essential medicines are in chronically short supply because they are not profitable to produce and/or have small, low-margin markets. For these, market-making consolidation of demand across borders and reduced disincentives for market entry are desirable. Local factors such as inefficient registration processes, rigid procurement regulations, poor demand planning, poor fiscal planning, and corruption can play a major role in determining which markets or sectors will be left short of products and which will not. While global and regional initiatives can support national efforts, these shortages are mostly the result of local problems that require local solutions.

## **Four questions raised by the research**

We hope that this paper will provoke debate among global health and development organisations about the pros and cons of adopting or supporting policies that affect the supply of quality-assured essential medicines in low- and middle-income countries to better respond to supply chain shocks such as the one caused by COVID-19. Considering the lessons of the research, and their potential policy implications, we raise the following questions:

### **1. Data availability and use**

Buyers can't react quickly to a potential supply shock if they don't know where a product and its ingredients are made. And yet the pharmaceutical market is unusually opaque. Data-driven approaches to guarding against the effect of supply shocks cannot be effective unless more transparency is introduced. But transparency is likely to be strongly resisted by industry. Some regulators and procurement agencies may also find greater transparency uncomfortable.

*What is the "minimum ideal" dataset for predicting shortages of a specific product in national markets? If these data were available to national regulators, would they use it proactively to signal potential shortages in*

*the supply chain? Who would lead the fight for greater transparency, which will be opposed by R&D and generic pharma alike?*

*What are the incentives and, especially, disincentives to standardise data on national production, consumption, imports, and exports of specific products, and share them through an internationally accessible platform? Is it politically feasible to share data internationally? What problems might internationally standardised data solve at the country level that can't be solved with data already or potentially available locally? Whose job is it to do that analysis and solve those problems?*

*Who would have to do the work of generating standardised data, and who would pay them? How much would it cost, and what are the likely benefits in terms of reduced shortages caused by supply shocks, taking into account all the other causes of shortages?*

## **2. Increasing redundancy in production and distribution**

The pharmaceutical industry maintains its efficiency (and thus its profitability) by "optimising"—often outsourcing to low-cost producers, and minimising stock on hand as much as possible throughout the supply chain. The optimised model also centres on large batch production, which achieves economies of scale but reduces adaptability.

Cost-cutting threatens quality and also reduces the ability to absorb any shocks in times of reduced supply or spikes in demand. Increasing redundancy in production capacity, and holding more stock throughout the system, would reduce the risk of supply shocks in times of crisis. Because this introduces inefficiency, it will increase the unit cost of production and storage. In consequence, producers and distributors will have to accept lower profits, or governments and other consumers will have to pay slightly higher prices, or both, all of the time. Countries that use their bargaining power well in procuring medicines (many of them wealthier countries with near-universal health coverage) now pay very low prices for most essential medicines most of the time, and high prices only in times of crisis. To those who can afford the surge pricing, this market model may be preferable to one in which increased redundancy raises prices for everyone, all the time, in an effort to ensure supplies to poorer clients in times of crisis.

*How much would increased redundancy for essential medicines add to unit cost of production and storage? Who will foot the bill? If prices rose as a result of increasing buffers to protect against supply shocks, might that effectively reduce access for the poorest countries and patients all of the time? If yes, could that outweigh any gains that result from a buffer for times of crisis? What hedging or other mechanisms might spread the cost of redundancy?*

## **3. Aggregating demand or pooling procurement**

Another way of achieving more balance between a global supply chain and local consumption is to aggregate purchasing at a supra-national level (for example regional or global), through pooled procurement. However, there are currently very few well-functioning inter-country pooled procurement mechanisms that buy a wide range of essential medicines procured principally by national governments. Those that do succeed tend to group relatively homogenous buyers who don't compete to produce medicines

themselves, and who already share structures that facilitate financial interaction. These mechanisms go far beyond being glorified e-commerce platforms; they provide a rounded (and potentially costly) service including revolving funds and support for demand planning.

*Why have existing attempts to establish multi-country pooled procurement of a wide range of essential medicines in sub-Saharan Africa not made more progress? Could the current efforts be replaced by e-commerce platforms that drive buyers to a limited number of quality-assured providers while providing price transparency? Who will pay for quality assurance? What governance structures would be necessary to ensure that contracts are honoured, including in times of heightened demand?*

*Who will support the regulatory harmonisation needed to make any pooled procurement model work outside of emergency situations? Is there any appetite among global health funders to support a third-party platform which provides the services currently associated with successful pooled procurement (such as demand planning services, maintenance of a rotating fund and buffer stocks) for essential medicines not currently covered by global programmes? How much would it cost and who would pay?*

*Could an externally sponsored platform over-ride national procurement regulations for medicines commonly bought by governments? What are the incentives and disincentives for governments to share control of their regulatory process with other countries through harmonisation? What are the incentives and disincentives for governments to entrust procurement of essential medicines to a third party?*

#### **4. Localising production**

The quest for low costs has effectively concentrated the production of high-volume, low-value pharmaceuticals (including many essential medicines) in just a few parts of the world. Most low-income countries are heavily dependent on imported medicines; the sub-Saharan African market is dominated by Indian generics made from Chinese active ingredients. Diversifying sources of supply, including by producing more within the African region, spreads the risk, so that if supply from one source dries up, other sources are available.

The development of production capacity in new geographical areas may have implications for cost or quality, especially in the early years.

*How feasible is it to harmonise trade, customs, quality, and market regulations in support of the goal of more production in those sub-Saharan African countries where infrastructure is already relatively well established? How would this affect the unit cost of medicines? Will importing from other sub-Saharan African countries increase security of supply in those countries not involved in the final production of finished medicines? What is the opportunity cost of this strategy? What are the likely sources of capital needed to implement the strategy?*

# 1. Introduction

Over the last two decades, access to affordable medicines has greatly improved for patients in middle- and many lower-income countries, thanks in large part to the joint efforts of national governments and their supporters in the global health and development sectors. Patient expectations rise in tandem with the volume of medicines consumed, producing concomitant concern about the risk of medicine shortages.

Shortages occur when the supply of a particular product in a particular location is less than clinical and “irrational”<sup>1</sup> demand combined. Shortages may occur locally or nationally, and sometimes also occur globally. The reasons for shortages are well-rehearsed. Demand may outstrip supply because of an unexpected increase in the number of people accessing services (for example, after an expansion of eligibility for public health insurance), or because of a disease outbreak. Inaccurate demand planning in the public procurement system can underestimate true need, leading to insufficient stocks being ordered. Efforts to push down prices in public procurement can lead to failed tenders, or can press margins so low that fluctuations in foreign exchange or price of raw materials make manufacturing or sales unprofitable, leaving orders unfulfilled. Cost-cutting can also lead to accidents which interrupt production, or to quality problems which lead to medicines being withdrawn from circulation. Natural disasters can stop factories from working; climate change is likely to lead to an increase in those disasters caused by extreme weather events, such as floods and wildfires. Politicians' efforts to assert themselves or their nation through military or trade wars can disrupt the production of medicines, or their flow from factory to patient.

None of these phenomena are new, although some appear to be increasing in frequency, the result of the combined effect of increased demand for low-priced medicines; the optimisation practices in production and distribution adopted to meet that demand; increasing nationalism in politics; and climate change.

Some mitigation measures for these long-standing challenges are already in place. Several countries require producers and/or market authorisation holders in their jurisdictions to report any foreseeable shortages, for example. However, these measures are less common in lower- income settings; the human and institutional capacity to respond to supply or demand shocks in those settings is also frequently limited. Indeed, panic triggered by shortages of personal protective equipment and some SARS-2 related medicines early in the COVID-19 pandemic, and the many variations on the March 2020 headline "Coronavirus exposes the weak links in the pharma supply chain"<sup>2</sup> suggest that the supply chain vulnerabilities remain a concern in countries at all levels of income.

The many discussions about shortages in global health circles have led to an increase in pre-emptive action for some commodities. For COVID-19 vaccines, for example, significant

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<sup>1</sup> This term is used to refer to demand for medicines that are not the most cost-effective clinically indicated product. It includes demand for medicines for recreational or other non-medical uses, as well as demand for specific brands or formulations in place of a more cost-effective therapeutic equivalent.

<sup>2</sup> Durbha, Madhav, Supply Chain Quarterly, 5 May 2020.

progress is being made in establishing transparency about production capacity, availability and source of raw materials, and procurement and distribution volumes, perhaps setting precedents for other therapeutic classes. For now, however, many countries still have much to do to build sustainable systems that will lead to persistent secure supplies of affordable, quality essential medicines.

## **Using the COVID spotlight to illuminate chronic challenges in medicine supply**

COVID-19 has turned the spotlight on supply chains, highlighting especially the challenges of ramping up production of COVID-19-specific products to meet a massive spike in demand, and the danger that richer countries will consistently outbid those with less ready cash when competing for the same resources.

It has also provided us with a great opportunity to learn about the effects of supply disruptions. It is rare that so many different sources of supply disruption arise at the same time: plant closures; shortages of labour, equipment, and raw materials; suspension of transport links; politically mandated export restrictions. It is rarer still that these are coupled with a demonstrable spike in global demand, are so well-documented, and are of relatively clear duration.

The wealth of information related to supply disruptions in the early months of the COVID-19 pandemic provides us with a learning opportunity, potentially allowing us to build and train models, or develop other tools that could be used in more “ordinary” times to predict the potential impact of disruptions to medicine supply on availability of medicine to patients in different markets, and to inform mitigation methods.

Shortages of essential medicines have received increasing attention from researchers, regulators, and the World Health Organization (WHO) in recent years. This interest has fuelled a few bodies of work examining the factors which contribute to medicines shortages and approaches that could be used to manage them.

Prominent among these is work by the WHO which is a member state notification-based warning system (WHO 2017). There is also a more recent EU project (cite MIA) to track medicine shortages in the UK, select EU countries, and Ethiopia. The literature examining reasons for shortages looks at supply disruptions due to manufacturing challenges, demand uncertainties, regulatory actions, and supplier market exit due to low profit margins (WHO 2016, IMS Institute 2011, GAO 2014, Gray & Manasse 2011, Fox et al. 2014, Conti 2011, Woodcock and Wosinska 2013, Bogaert et al. 2015, Pauwels 2014). USP has initiated work recently to understand risks in the upstream medicine supply chain by looking at information about the locations of API (active pharmaceutical ingredient) manufacturing sites and a number of other data elements.

A number of strategies have been proposed to prevent drug shortages (Tucker et al. 2019, Gray 2014, WHO 2016), which include requiring purchasers and pharmaceutical companies to build redundancies, mandating that purchasers and procurers use failure-to-supply clauses,

improving manufacturing and regulatory processes, and expanding and improving information sharing and reporting systems. There is also a vast body of literature on supply chain disruptions that provides operational details on sourcing contracts to mitigate supply disruption risks (see Pourmader et al. 2020 for a recent review of such literature).

The COVID-19 pandemic has also brought new focus and attention to understanding the risk of supply disruptions, both upstream and downstream. Global agencies such as the Global Fund which finance medicines for HIV/AIDS, TB, and malaria and organizations which fund contraceptives have initiated new workstreams to understand the risks of supply disruptions. In particular, the Reproductive Health Supplies Coalition (RHSC) (with technical support from JSI) has initiated work to understand COVID-19-related risks of supply disruption by leveraging different data sources.

While each of the above are important bodies of work, and some of them have informed our work, none of these get into an analytical framework for bringing together data of different types (qualitative and quantitative) and from different sources (wholesaler surveys, trade data, retail data) to estimate the risk of shortage for essential medicines which are funded by low- and middle-income country (LMIC) governments themselves.

Some of those efforts focus on avoiding shortages in higher-income markets; others on specific classes of products, generally related to COVID-19 itself, or to other diseases or health issues of particular interest to large global health initiatives such as the Global Fund, GAVI, UNITAID and other programmes funded by USAID, the Bill and Melinda Gates Foundation, and other development agencies.

We have no wish to duplicate existing work. This paper instead raises issues related to a subset of 64 other essential medicines, selected as described below. As their name suggests, essential medicines are vital to the well-being of large numbers of people in most countries, including those with limited resources. However, their procurement and distribution are largely unsupported by the extensive infrastructure that has grown up around contraception, vaccines, and treatment and prophylaxis for a handful of infectious diseases—a group of commodities we refer to in this paper as “programme medicines.” In countries at all income levels, most non-programme essential medicines are sourced and paid for by national governments in the public sector. In the private sector, patients themselves most often pick up the tab, especially in lower-income settings where private health insurance is rare. Few if any governments get external support for condition-specific surveillance, demand planning, or procurement related to most essential medicines or the diseases they treat. It's likely, then, that the supply chain-related challenges for these medicines differ from those that absorb the attention and resources of the global health industry.

## **Purpose of this paper**

This paper summarises learning arising from work undertaken between April and October 2020 by the Center for Global Development together with analysts from a number of other organisations (see box 1 for a list of available background papers). Our aim was to use data collected from several different sources in the periods before and during the COVID-19

pandemic to better understand whether this crisis affected the of supply of medicines not directly related to COVID-19 care.

Using data across a number of essential medicines, we asked:

1. Would it be
  - a. possible
  - b. usefulto use data to provide early warning of potential shortages caused by supply disruptions?
2. If yes, what could global health organisations or countries do to
  - a. support the early warning systems
  - b. support systems for acting on those warnings?
3. Even if data-driven early warning systems are not possible or useful, what could global health organisations or countries do, if anything, to mitigate the predictable causes of interruption to the supply of essential medicines in LMICs?

This paper provides a brief overview of the results of efforts to answer question 1 above. It does not provide solutions or firm policy recommendations in answer to questions 2 or 3. Rather, it summarises areas of learning, and raises questions about the policy options suggested by that learning. We hope to provoke debate among global health and development organisations about the pros and cons of adopting or supporting policies that affect the supply of quality-assured essential medicines in LMICs. We recommend that readers with limited time focus on Sections 3 and 4 of the paper.

#### **Box 1. Research undertaken as part of this project**

This project was led by CGD but involved research by many partners, available at the links below.

[Press and data scan, Chinese API exports](#)

[Press and data scan, Indian manufacturing of finished products](#)

[Post-COVID-19 health commodity shortage tracking using the Maisha Meds network and Indian export data](#)

[Legal restrictions on exports of APIs and medicines, and travel disruptions caused by COVID](#)

[Country-specific reliance on imports from India](#)

[Survey of medicine wholesalers](#)

[Survey of central medical stores](#)

[Shortages detection model](#)

[Assessing alternatives for the expansion of medicine production in sub-Saharan Africa](#)

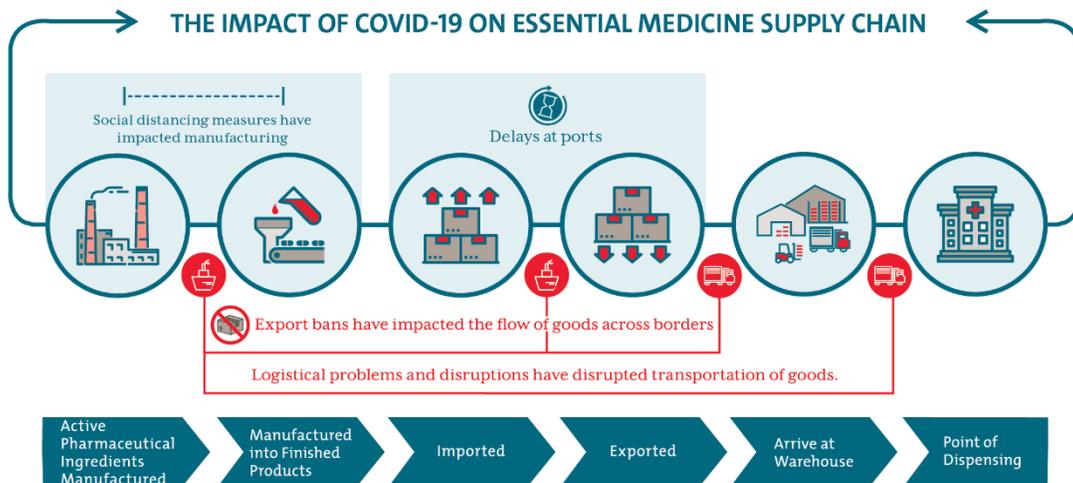
## 2. Analytic framework and analyses

A medicine supply chain starts with the production of raw materials—excipients as well as active ingredients—and packaging material. These various materials may be made at different times in different countries or locations, but in most cases they must all be available at the same time at the point of production of the finished product. The finished product must then travel (often across a number of international borders involving taxation and other paperwork, and through a number of different warehouses) to the point at which it will be dispensed to patients.

In today's complex and globalised supply chains, disruption at any point—shortage of glass vials, or an explosion at a monopoly producer of active ingredient, for example, or failure to secure the timely release of a shipment of medicines from customs because of non-payment of some questionable fee—potentially cascades through the chain to reduce shipments to the health care facilities, pharmacies, or market stalls which provide medicines to patients.

In the case of COVID-19, as shown in Figure 1, some disruptions were immediately obvious—national lockdowns shut factories or restricted the flow of labour; transport became scarce and more expensive; some countries simply banned the export of certain chemicals or medicines.

Figure 1. Supply chain flow chart



Our task was to try to quantify the effect of these shocks on the availability of the products under investigation, in the countries under investigation, and to use those data to try and build, calibrate, or test models that might flag supply shocks and/or predict supply-driven shortages in regular markets.

## **Rationale for product selection**

We focused on essential medicines not supported by large international access efforts because, as explained above, the ways in which they are produced and procured tends to differ significantly compared with programme medicines. Since we aimed to test predictor models for shortages, we proactively sought to include products at high risk of shortage. To this end, we performed a preliminary data scan to identify medicines with a highly concentrated supply chain, which increases the systemwide risk of failure at an individual company, or a lockdown or export ban in a single region. We also included those for whom trade data indicate significant fluctuations in price or volume, which may indicate either supply shocks or demand spikes.

The result was a list of 64 medicines (by molecule and formulation but not dosage). These are listed in the Appendix, Table 1.

## **Rationale for geographic selection**

We are interested principally in the effect of supply shocks on the availability of essential medicines in low- and middle-income countries, especially in sub-Saharan Africa where the ability to absorb price increases may be more limited than in other regions. We thus chose to look for evidence, quantitative if possible, of disruptions to production of finished products in India, which is the biggest single source of generic medicines to most countries in sub-Saharan Africa, as well as to many other low-income countries. Since Indian generic producers rely on China for many of their active pharmaceutical ingredients (APIs), we also attempted to collect evidence of shocks to API production in China.

In terms of shortages at the point of consumption of finished products—those described in sections B-D below—different analyses used slightly different mixes of countries, guided principally by the availability of data and the nature of the analysis. All included countries in sub-Saharan Africa. One shortage prediction model was additionally validated on countries in East, Central, and South Asia; Latin America and the Middle East and North Africa. The Appendix, Table 2 gives an overview of the countries involved in each analysis.

## **Overview of analyses**

Working with various research partners, we performed a number of different analyses. We attempted to

- A. Quantify upstream supply disruptions in China and India
- B. Directly measure shortages of essential medicines in study countries
- C. Further estimate shortages of essential medicines in study countries
- D. Develop models to predict likely shortages in low- and middle-income countries
- E. Aggregate risk scores
- F. Assess the potential for increased production of essential medicines in sub-Saharan Africa

Here, we sketch the types of analyses performed, and provide a brief indication of the outcome of each. We discuss the overall learning from this body of work in more detail in **Section 3** of the paper.

### **A. Quantifying supply disruptions; producers**

We attempted to collect data on supply disruptions of active ingredients from China, as well as finished medicines from India, in a number of ways. In addition, we attempted to verify our assumptions about the importance of geographic concentration as a source of vulnerability by measuring the extent to which countries of interest depend on imports from India as a source of essential medicines of interest. We performed the following analyses:

#### *A1. Press and data scan, Chinese API exports*

Full report [here](#).

A Mandarin-speaking analyst searched in academic and industry reports, regulatory and other official channels, and press reports for quantitative or qualitative information on changes in volumes of **Chinese production and export of APIs**, including factory closures, export bans, travel bans, and transport disruptions.

**Results:** Hubei province, whose capital Wuhan recorded the first outbreak of COVID-19, is among the largest producers of pharmaceutical chemicals in China. The lockdown dented production there more than in other provinces. The government strongly encouraged compensatory production in other sites. The consensus of industry insiders, as well as corporate profit projections, suggest that the impact of shortages on total volumes of API exported was short-lived. Expectations of rising revenues at many companies outside of Hubei suggest they increased production volume to compensate for shortfalls caused by lockdown, or that price rises outstripped shortfalls in volume, or both.

#### *A2. Press and data scan, Indian manufacturing of finished products*

Full report [here](#).

A Hindi-speaking analyst searched in academic and industry reports, regulatory and other official channels, and press reports for quantitative or qualitative information on factors affecting **Indian exports of medicines to other countries**. These included imports of APIs, API stocks maintained by producers, production and export of finished products, factory closures, export bans, travel bans, and transport disruptions.

**Results:** India is entirely dependent on China for 53 APIs/key starting materials, and heavily dependent for many more. Fourteen of these are molecules used in the formulation of essential medicines of interest in this study.

In March 2020, API imports from China were down by 24 percent compared with March 2019. However, most major producers of finished products have specific policies to increase buffer stocks of Chinese APIs at times of predictable disruptions, such as the Lunar New

Year, which coincided with the outbreak of COVID-19 in China. Larger companies maintain API stockpiles sufficient to keep plants running for 90 days at all times.

Although transport links were disrupted by the pandemic, a border dispute with China probably also contributed substantially to delaying resupplies of Chinese API. Ultimately, few serious stock-outs were reported, although prices of many molecules rose by up to 30 percent, in part because of rising freight costs. Industry executives reported speculative hoarding of stocks on the part of distributors hoping to benefit from price rises, but it was not possible to confirm this with quantitative data.

Pharmaceutical companies were exempted from lockdown in India, but poor coordination between levels of government and between states shackled the workforce and restricted access to key raw materials. The Pharmaceutical Export Promotion Council of India reported that exports of generic formulations fell by 19 percent in value in March 2020 compared with a year earlier, compared with 14 percent growth in January and 9 percent growth in February.

### *A3. Change in Indian manufacturing of selected finished products*

Full report from Maisha Meds [here](#).

We estimated **changes in manufacturing in India** by combining two datasets. The first was generated by working with business-to-business pharmaceutical network Pharmarack to estimate sales and inventory of target medicines within India.

The second was compiled by Maisha Meds from customs data reported by line item, detailing the volume and value of the medicines and formulations in an export cargo from India, by destination. Indian export records are among the world's most complete. However, as is often the case with pharmaceuticals, volume data are problematic. While standardised pharmaceutical market data report volumes by smallest counting unit (e.g., tablet, vial or 5ml dose of syrup), customs data use a variety of volumes—boxes, bottles, cartons, etc.—often of undisclosed size. This means that volume must often be imputed from value, a process which is time-consuming and sometimes inaccurate, not least because tax rebates to incentivise exports from India may lead to overstatement of value. However, volumes were calculated as accurately as possible for the essential medicines of interest.

We assumed that all medicines made in India are either consumed, held as inventory, or exported. We inferred changes in production in India from the change in domestic inventory over a month, after subtracting domestic sales and exports in that month.

**Results:** We estimated that, having risen from 21 million manufacturing units in January 2020 to nearly 26 million in February, the output from Indian pharmaceutical plants crashed by 44 percent to below 18 million, before recovering in April and May to around 22 million.

#### *A4. Legal restrictions on exports of APIs and medicines*

Full analysis [here](#).

We collated information on **export bans and export licensing requirements** relating to the medicines of interest from the Global Trade Alert database, which records national legislation and regulation relating to trade, including export and import licensing requirements, export and import bans, and other acts which affect the flow of goods between countries. Because medicines can be shipped through third countries, we included all countries in this analysis.

**Results:** Globally, 46 trade-related restrictions were placed on medicines in 2020 (far more than the 5 recorded in 2019). The most salient of these came from India, which in March 2020 briefly banned or restricted the export of 26 medicines in acute demand because of the COVID-19 pandemic. Three of these, acyclovir, metronidazole, and Vitamin B complex, were among the molecules of interest in this study.

#### *A5. Reductions in shipping capacity*

Full analysis [here](#).

We analysed data related to **air freight and shipping** provided by Agility, a logistics information company with expertise in supply chains in emerging markets, to look for disruptions which may interrupt the flow of medicines to our markets of interest. While API and many finished products are shipped by sea, air freight is commonly used to ship low volume, high value items, as well as lower-value essential medicines when a shortage exists or is looming.

**Results:** Both air freight and sea cargo were significantly disrupted in the early months of the COVID-19 pandemic. Air freight from China to India was reduced by 90–100 percent throughout March and April 2020, and remained constrained for much of May and June. For sea freight, data are not available by country of destination, but capacity was constrained from China to all Asian destinations until at least the end of July.

Meanwhile, air freight from India to all regions except for the Middle East was reduced between 90–100 percent until the end of June 2020. Sea freight to Africa was normal or partly limited until mid-April 2020, and was then significantly constrained until late May.

#### *A6. Exports from India*

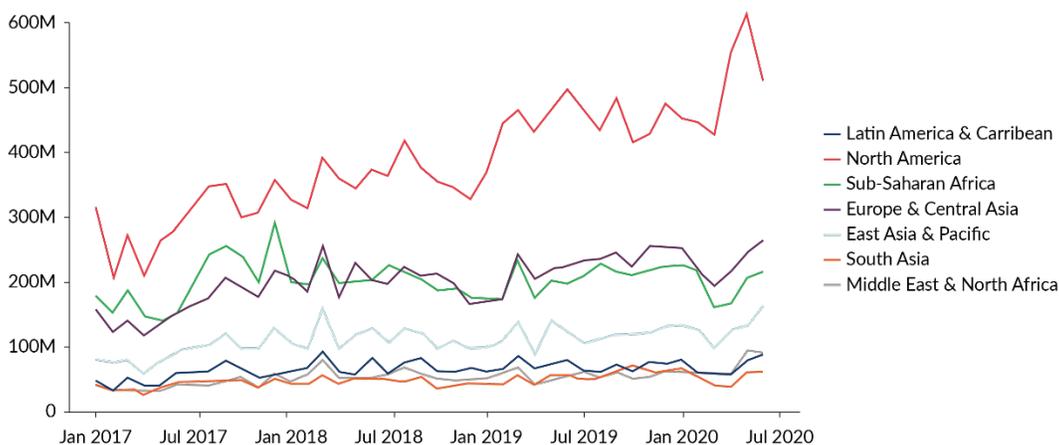
Full report from Maisha Meds [here](#).

Maisha Meds further analysed the database constructed from customs records (see **A3**). In customs data relating to pharmaceuticals, value data tend to be more robust and comparable than volume data. Though they may suffer from bias because of over- or under-declaration, this bias is unlikely to change dramatically over time. Analysts thus examined patterns in the

total value of export shipments, looking for changes over time in exports to specific countries, and for signals of relative changes in distribution of exports between regions.

**Results:** Figure 2 shows the declared value of exports of the study products from India between January 2017 and July 2020. Monthly fluctuations are common. However, exports to all markets dropped markedly in early 2020, with the exception of the Middle East (the only region to which shipment was not constrained, according to the Agility data). There followed a rebound, seen most strongly in exports to North America, although these had normalised by mid-year. Since this graph shows value rather than volume, the sharp rise in exports to the US may reflect the willingness of importers in that market to pay over the odds in a time of real or perceived threat to supply.

**Figure 2. Change in the value of finished pharmaceutical monthly exports from India to each global region, Jan. 2017–June 2020, in US\$**



*Source:* Indian export data.

#### *A7. Country-specific reliance on imports from India*

Full analysis [here](#).

Attempts were made to estimate the reliance of some low- and middle-income markets on imports from India by comparing data on the volume of exports from India to a specific country with total market volume in that country (IQVIA market data). A further attempt was made to match export data from India with import records from a single country, Kenya, known to have strong links with India in its pharmaceutical sector.

**Results:** The data on export volumes from India as currently available are not sufficiently complete to allow for reliable estimates of export volume at the country level. In addition, while data on volumes of medicines sold in the private sector in some African markets is improving in a few countries, the public sector remains opaque in most countries, making it difficult to estimate the total size of the national market against which to compare Indian

export volumes to ascertain dependency. Kenyan import data proved even less granular than Indian export data.

## **B. Survey-based assessment of shortages in focus countries**

From a public health point of view, supply disruptions are important principally because they can lead to shortages, thus depriving patients of the care they need. In order to develop and test the models described in section D, we needed to have some idea of the possible links between disrupted supply and shortages in markets of interest. We attempted to measure shortages in the following ways:

### *B1. Survey of medicine wholesalers*

Full report [here](#).

Pharmaceutical data and analytics specialists IQVIA conducted a **survey of 27 medicine wholesalers** and distributors in six countries in August 2020. They asked distributors which of the products of interest were currently out of stock, or were expected to be in shortage soon, and checked those reports where possible against inventory and existing orders.

**Results:** Reported stockouts or expected stockout were quite common, although curiously, when we checked these reports against inventory, there was often enough stock in hand and on order to cover historical demand. Most notable was the lack of consistency between and even within countries about what was in short supply. No product was reported as being in short supply in all countries. Within a given country, agreement was also rare; in only one instance was a product reported as in shortage by all the wholesalers who would normally stock it. This suggests quite a healthy diversity of supply, and does not support the hypothesis that stockouts were the result of an upstream shock severe enough to create global shortages.

The most common reasons given for stockouts were the inability of wholesalers or manufacturers to provide supply. In one country, the inability to acquire foreign exchange to pay for goods was also mentioned repeatedly.

### *B2. Survey of central medical stores*

Full report [here](#).

Procurement consultants TalaConsult conducted a **survey of central medical stores** in sub-Saharan Africa. Ultimately just one subnational and four national stores completed the survey, reporting on current and expected stock-outs across those products of interest which are publicly procured in each of the countries.

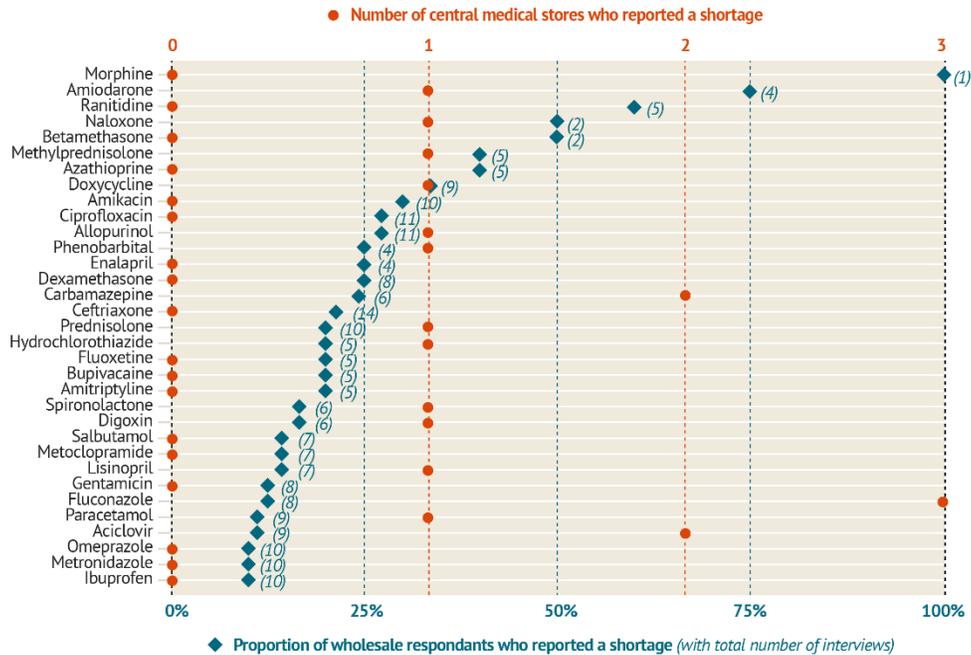
**Results:** Responses were lower than we hoped. The heads of three of the national medical stores we had targeted for a survey were either in jail or under investigation for alleged procurement irregularities, economic sabotage, or financial mismanagement of COVID-related procurement at the time of the survey. This suggests that extreme disruption of

global supply and/or demand increases opportunities for mismanagement and corruption, while perhaps simultaneously increasing scrutiny of medicine procurement, increasing the likelihood that wrongdoing will be detected. It also raises questions about public procurement regulations; if these are overly restrictive, officials may be unable to respond rapidly to demand or supply shocks without breaching rules.

The diversity of shortages reported by the central medical stores that did participate was similar to that reported by wholesalers. In total, 50 of the study products were normally stocked by at least one of the countries with national stores (Gambia, Malawi, and Senegal), and 17 of them were reported to be in shortage by at least one country. However, shortages are a regular occurrence in most central medical stores, and they have strategies in place to respond. For 64 percent of the products in shortage, replenishments were expected within the next three months. Figure 3 compares the frequency of stock-outs reported in the survey of wholesalers with the availability of the same products in the reporting central medical stores.

It is notable that some of the products most frequently unavailable from central medical stores seem to be easily available to wholesalers. Meanwhile, products not usually stocked by any of the wholesalers surveyed were in good supply at medical stores. Respondents suggested that this may be because government pharmacists prioritise resolving shortages for products that patients could not easily access in the private sector, often because the private sector does not import them.

**Figure 3. Supply chain shortages as identified by wholesale and central medical store surveys**



### **C. Estimating supply disruptions to low- and middle-income countries using export and sales data**

Besides the direct measures reported above, we attempted to estimate supply disruptions from changes in volumes and in prices in medicine retail data collected from a variety of sources. Since changes in sales volumes and prices are a function of demand as well as supply, these data do not directly measure supply disruptions. Market logic suggests that abrupt drops in sales volume or hikes in price of a commodity, and in particular the combination of both of those factors, may be caused by a shortage of supply. The extent to which this is true of medicines is open to question—in many markets, prices are controlled, while seasonal variations in demand are common for some medicines, especially those that treat infectious diseases. If volumes fall and prices rise across markets, confidence grows that supply constraints are likely at work. We thus explored these factors across a range of countries.

#### *C1. Comparing changes in price and volume of exports from India*

Full report from Maisha Meds [here](#).

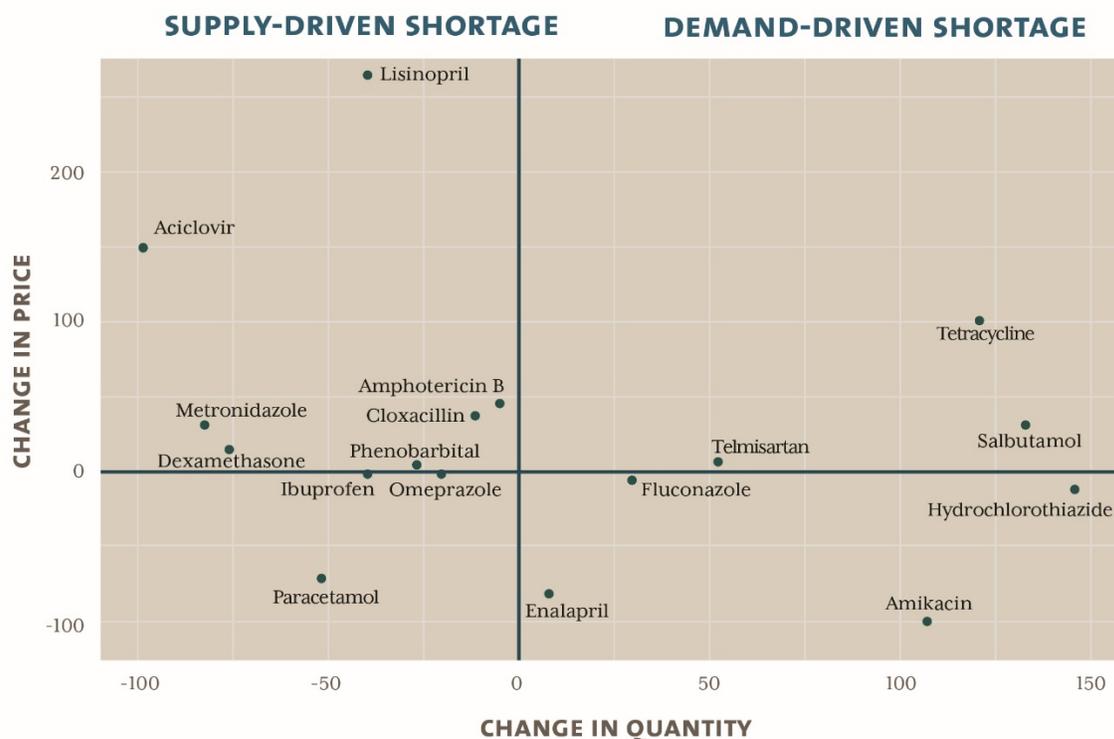
For the Maisha Meds database constructed from customs records (see **A3**), value was divided by volume to ascertain price, and changes in average monthly value, volume, and price were calculated for a selection of 60 products, comparing the two-month periods before February 2020, the start of the global COVID-19 pandemic, with the three months of March-May 2020.

If exports of a medicine fall, but the price also falls, it is probable that demand for the product has dropped off, or is being satisfied from other sources. If, however, the price rises while exports fall, it is more likely to signal scarcity. For medicines of interest, analysts compared the changes in volume of exports to sub-Saharan Africa between the pre-pandemic and pandemic periods with changes in value over the same time.

The robust calculation of volume depends on useable information on pack sizes, which is not always available. The volume data were thus not available for all shipments; this analysis compares volume and price only for shipments with robust volume data.

**Results:** Figure 4 compares changes in volume (on the horizontal axis) with changes in price (on the vertical axis). In the top right quadrant are products which rose in both price and export volume. For these products, then, rising prices do not appear to signal scarcity. Those in the top left quadrant, however, saw lower volumes of exports, at higher prices. These are the products most likely to be in shortage. This is based on extremely limited data, so results are indicative only.

**Figure 4. Average monthly % change in price and volume of exports of different molecules from India, comparing March–May 2020 with Dec. 2019–Jan. 2020**



The inferences drawn here about demand vs supply are indicative only and based on small data

**Results:** Table 1 gives details of the number of products for which prices rose or fell, by the change in volume.

**Table 1. Molecules exported from India to sub-Saharan Africa, by change in average monthly price and volume comparing March–May 2020 with December 2019–Jan 2020**

Change	Number of products (%)
Price rises, volume falls	7 (41.1)
Price rises, volume rises	3 (17.6)
Price falls, volume rises	4 (23.5)
Price falls, volume falls	3 (17.6)
Total	17 (100)

The 41 percent that saw lower volumes of exports at higher prices—the first row in the table—are the products most likely to be in shortage. The price of the three products in the second row also rose, but since volumes rose too, it seems unlikely that rising prices signal scarcity.

For the three products in the bottom row of the table, falling volumes accompanied by falling prices may signal that demand dropped more than the market anticipated, perhaps because of restrictions on movement and access to services associated with the pandemic. However, the relationships are not always straightforward. One of the molecules in this last category, in which prices fell in tandem with supply, was paracetamol, a normally fast-moving molecule on India's export restriction list. One possible explanation for the drop in price is that higher value (and less common) formulations were disproportionately affected by shortages, leaving the average price for shipped products lower. It underlines the difficulty of interpreting aggregated data in the complex landscape of pharmaceutical products and formulations.

## *C2. Change in retail sales of study medicines in four countries*

We compared retail sales for study medicines in Ghana, Nigeria, Kenya, and India. Although reduced demand is also a possible cause, we hypothesised that similarities in reduction in sales volumes across all markets (including India) might indicate a reduction in manufacturing, while similarities across African markets only would be more likely to reflect transport constraints, export restrictions, or redirection of Indian sales to other regions.

mPharma, a Ghana-based healthcare technology company that manages pharmaceutical inventory on behalf of pharmacies across Africa, shared sales data for the target medicines from Ghana and Nigeria from January 2019 to May 2020. Maisha Meds was able to provide similar sales data for Kenya. Pharmarack provided data for India.

**Results:** Comparing average monthly sales in the year prior to COVID-19 with those in March, April and May, when the effects of any market shocks might be felt by consumers, no clear picture emerges. Changes in both inventory and sales volume varied considerable between markets, even for the same products. In terms of changes in inventory in Indian pharmacies between April and June 2020, for example, inventory was largely unchanged or increased by up to 100 percent for roughly half the molecules of interest, suggesting lower sales. The other half saw inventory decrease by up to 65 percent. Sales of the epilepsy drug carbamazepine rose by 140 percent in Ghana while plummeting by 90 percent in Nigeria, while antibiotic ceftriaxone showed the opposite pattern. In Kenya, the number of products for which prices to supplier rose peaked in April (led by demand for medicines thought to be useful against COVID-19), but there was no major change in stockouts among wholesalers during the study period. Analysis of data collected by Maisha Meds beyond the end of the study suggested that the number of products in shortage in Kenya peaked in July, several months after any supply shocks at the level of production.

## D. Developing models to flag potential supply disruptions

Analysts developed and tested two models designed to provide real-time flags for potential supply disruptions. Model development, which included trial and refinement of various approaches, is described in detail in the full reports to which links are provided. Here we give only a very brief overview of each of the final models.

### *D1. Shortage Detection Model (IQVIA)*

Full report [here](#).

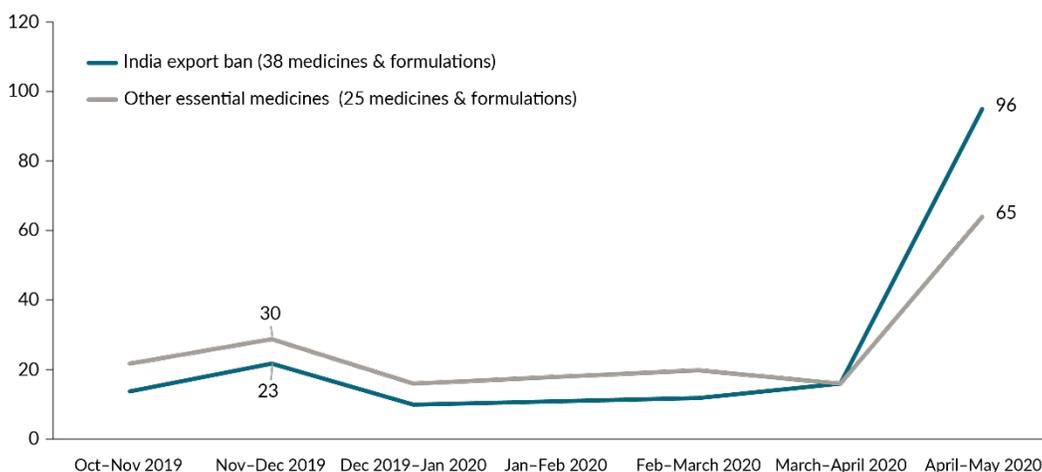
IQVIA developed a "Shortage Detection Model" trained on data from Germany and Canada, then tested it against data for 22 low- and middle-income countries. Analysts first used historical data from a small subset of products in Germany, where manufacturers are obliged to report expected shortages, to predict sales forecasts over one to two months for reported products, using three different methods. The prediction methods were then used to forecast sales for all other products reported to be in shortage in Germany, together with a set of controls (products not reported as being in shortage). There were 10 times as many controls as shortage products.

Next, predicted sales were compared to actual sales volume. A significant difference between predicted and real sales creates a "shortage signature," a signal that a product is possibly in shortage. Analysts recorded the number of products correctly identified as being in shortage and the number correctly identified as not being in shortage, comparing them with those incorrectly identified, to find the best fitting model. To test whether these same forecasting methods were applicable outside of Germany, the same methods were used on historical data from Canada, another country that requires reporting of expected shortages.

Based on the results of that validation, analysts selected the most accurate method (exponential smoothing for time series, or ETS) and applied it to data from 22 low- and middle-income countries, to predict what sales would have been in the absence of the pandemic. One product group consisted of those products that India briefly banned from export; the other set consisted of other essential medicines of interest. Again, predicted sales were compared to actual sales. If the actual volume was below the lower bound of an 80 percent confidence interval around the expected volume, the product is flagged as possibly in shortage at that time.

**Results:** We hypothesised that there would be more products flagged as possibly in shortage in the pandemic period than in the pre-pandemic period, and that the difference would be greatest for the products affected by India's export ban. This was broadly true: overall, we found 161 instances of unexpectedly low sales in the April-May 2020 period, compared with a high of 53 in any previous two-month period going back to October 2019. (Figure 5) Only 16 of 63 products (molecules by formulation) were not flagged as having lower-than-expected sales in any country in the April-May period.

**Figure 5. Number of potential shortages flagged by the Shortage Detection Model by two-month period, 22 low- or middle-income countries**



*Source:* IQVIA retail market data

Interestingly, there was limited consistency between markets at the period of peak "shortage" covered by the analysis (April and May 2020), as well as limited consistency between different formulations of the same molecule. No product was flagged in more than half of the 22 countries. Rectal formulations of paracetamol, a molecule that was subject to an Indian export ban, appeared most affected, with 11 countries showing sales below the 80 percent confidence bound of those predicted. However, paracetamol pills or capsules, by far the more commonly used product, sold less than expected in only two countries.

Of course, an unexpected drop in sales may equally signal lower demand; this is especially likely during the early months of the COVID-19 pandemic, when many people curtailed their movement. That reduces the value of the model as an indicator of supply shocks. From a public health point of view, however, the model retains its utility. To the extent that people buy medicines for which they have a therapeutic need, lower demand probably also signals unmet need, at least for medicines for chronic conditions.

#### *D2. Trend Break Model (Maisha Meds)*

Full report from Maisha Meds [here](#).

Maisha meds conducted a similar prediction exercise using different data and methods. Using the monthly Indian export values since January 2017 in the customs database described in **A3** and **A6**, analysts used an AutoRegressive Integrated Moving Average (ARIMA) model to forecast the expected export values aggregated from all sub-Saharan African markets (except the regionally atypical South African market) after February 2020, in the absence of any pandemic effect. These forecast exports were then compared with actual exports to the region in the post-pandemic period (the four months from February 2020). Unexpectedly sharp drops in export value were identified for 116 out of 525 products.

The products flagged as potentially in shortage based on lower-than-expected value of exports from India to sub-Saharan African markets were compared with products reported to be in shortage in the wholesaler survey.

A further attempt to use the trend break model to flag potential shortages in exports from India to Kenya historically, and to compare the outcomes with retail prices from Kenyan pharmacies.

**Results:** The model flagged half of the molecules confirmed as being in shortage by local wholesalers. It performed better when looking at molecules with robust Indian export data for active ingredients. It also flagged many molecules that were not reported as being in shortage. Overall, the model did not perform well enough to accurately flag country-level shortages of finished products.

Resource constraints to clean and then analyse a largely unstructured dataset hindered this analysis. In particular not having time to build stronger data cleaning algorithms, only having an 18-month time series for API export data, relying on value change as a signal of shortage, and only having access to Indian export data (representing 33 percent of exports to sub-Saharan Africa by value) were the key constraints to this analysis. Difficulty in accurately calculating volume and form for many products, due to inconsistent data capture from Indian ports, is a serious impediment to future implementation of this methodology at scale.

### **E. Aggregating risk scores**

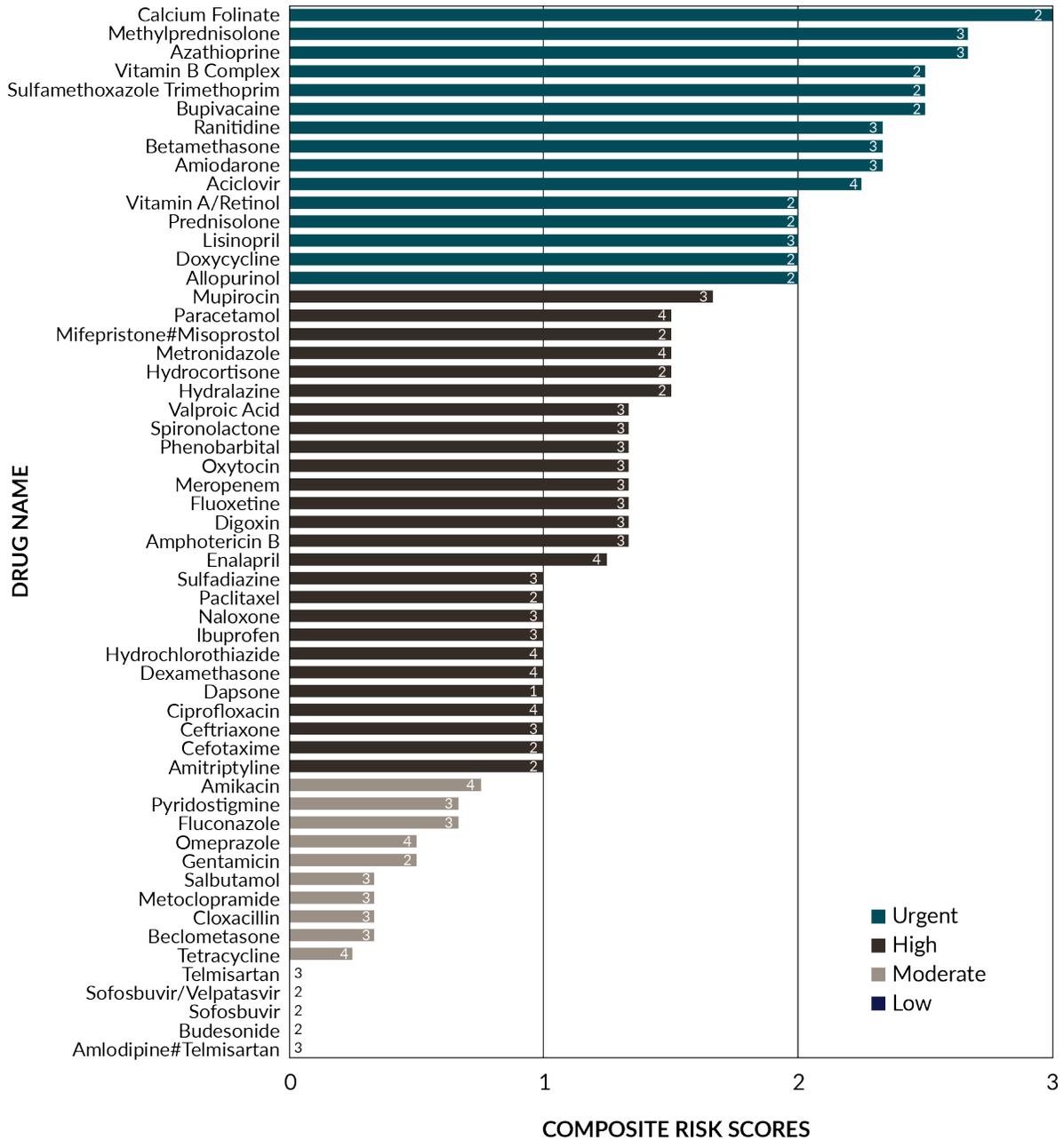
We cast a wide net when looking for data sources to maximise the information we had about the drugs in our tracer list, as well as to learn more about the different data sources. To compare these sources we analysed four datasets, including pharmaceutical retail, wholesale, and export data that were collected from our partners Maisha Meds, Pharmarack, and IQVIA. We used these data to generate composite risk scores for individual drugs, to understand whether drug shortages are demand versus supply driven, and to assess which countries are most significantly impacted by drug shortages.

Each drug was ranked from “urgent” to “low” priority based on the relative decrease in exports from India, retail sales in India, predicted drug shortages (using IQVIA’s prediction model), and wholesaler interviews. We then took the average of these individual scores to generate a composite risk score.

**Results:** The correlation in individual risk scores from the different models is not always high, ranging from 0.06 to 0.41. Low correlation would indicate that the different datasets may be capturing information about shortages from different parts of the supply chain and are therefore complementary. However, given that all datasets did not capture full information about all drugs, that each data set uses a very different methodology which can be difficult to compare, the different data sets capture information on different drugs, as well as the limitations for each specific data set outlined already. The low correlation could therefore be due to limited data.

**Key takeaway:** An approach which integrates data from different levels in the supply chain can be a useful way to understand overall risks of shortages. Robust analysis requires refining data collection processes, ensuring access to high-quality data across different parts of the supply chain.

**Figure 6. Composite risk score, shortage by data source**



## F. Assessing alternatives: The expansion of medicine production in sub-Saharan Africa

Full report [here](#).

Because many countries in sub-Saharan Africa are heavily dependent on medicines made in India using ingredients imported from China, most of our analyses focused on the flow of active ingredients and essential medicines through a globalised supply chain. As a corollary to that body of work, described in sections A-D above, we also looked at the feasibility of reducing that core dependency by producing more medicines within the sub-Saharan African region. Pharmaceutical industry consultants Bryden Wood estimated the capacity that would be required to produce 100 percent of the essential medicines of interest needed by sub-Saharan Africa within the region itself. They then used their own sector expertise to assess the feasibility of building that capacity.

**Results:** The assessment suggested that production of oral solid formulations (tablets, capsules, caplets) may be feasible, but that developing capacity for other formulations would be more challenging. With little legacy manufacturing infrastructure in place, some nations would be well placed to leapfrog traditional, high-volume batch production, and instead build from scratch the capacity to use lower-volume, and more flexible, continuous production models. The analysis recommends a hub-and-spoke model, with higher-tech functions initially concentrated in a few areas with existing infrastructure and transport links. Spokes in less-developed areas would build up infrastructure and capacity gradually, starting with less technically demanding tasks such as packaging.

In this model, products and components must cross borders, so a high degree of coordination, including on issues such as tariffs and product registration, would be necessary.

## 3. Summary of learning

Between them, the analysts working on this project were able very quickly to draw together an extraordinary volume and variety of data across a number of countries. We found clear indications of reduced volumes and increased prices of APIs imported to India; reduced volumes of some essential medicines manufactured in India; limited availability of cargo transport from India; and reduced value of exports of some essential medicines from India to countries of interest. Almost all of these disruptions appeared short-lived, with clear signs of a rebound to "normal" levels for most indicators towards the end of the study period (May/June 2020). For a handful of molecules in one market, we found some evidence that lower imports from India, in value terms, was followed after a lag by higher retail prices. Overall, however, the indications of disrupted supply from the world's largest exporter of essential medicines in finished form were not tidily correlated with shortages of those medicines in the lower-income markets we looked at, by any direct or proxy measure. Possible reasons for this include some combination of the factors listed here:

### **A correlation exists, but our analyses could not capture it because**

- the data are poor quality;
- the data are incomplete, or lack the necessary granularity;
- the data are too noisy: the natural fluctuations in supply as well as other causes of shortages drown out signals that would reliably predict shortages from manufacturing and trade data alone;
- the link between global supply shocks and local shortages plays out very differently in different markets, so that no pattern can be discerned
- buffer stocks and procurement timelines pushed the effect of any supply shock at the retail level beyond the time period captured in our analysis.

### **No correlation exists because**

- the supply shock was too short to have a measurable effect;
- the global pharmaceutical supply chain is more resilient than we anticipated;
- demand dropped at least as much as supply.

## **Key lessons**

The exercise of comparing data from different sources across the length of the supply chain—from API production in China, through manufacturing of finished products in India, shipment to wholesalers and central medical stores in lower-income countries, and ultimately retail sale—was useful in highlighting issues worthy of consideration by national governments as well as the global health organisations that seek to support them. They include:

### **Politics and governance matter**

A lot of the discussions about supply chains have focused on the technical aspects of production, procurement, and supply planning. But COVID-19 has served to strip naked the fact that national or more local politics can affect trade just as much as the raw market forces of supply and demand.

In China, for example, state ownership of some major pharmaceutical producers, combined with a relatively centralised government and strong state influence on companies, likely affected the speed at which companies in regions other than Hubei were able to compensate for the shortfalls in production occasioned by the lockdown in that state.

Political power in India, on the other hand, is much more devolved. This creates a different set of vulnerabilities. Baddi, in Himachal Pradesh, accounts for 35–40 percent of India's output of finished medicines, and over a third of Asia's imports. But efforts of the local government to keep factories running at capacity were thwarted because many of their workers live in neighbouring Haryana and Punjab and were not allowed to cross state borders.

In addition, it appears that the disruption of supply of APIs from China to India in early 2020 was at least in part the fall-out of increased political tensions associated with the border dispute.

Obviously, then, it is not enough to think only about geographic concentration of different elements in the supply chain. The political landscape and institutional structures governing those areas of geographic concentration have a material influence on the level of risk associated with the concentration, just as risk of flooding, forest fires, or earthquakes do.

National interest also affects some of the possibilities for reducing concentration in supply. The hub-and-spoke model for production within sub-Saharan Africa, for example, depends on a high degree of cooperation between countries included in the production networks, and good relations between network and importing countries. These can easily be compromised by political conflict.

Governance is also an issue. Corporate and regulatory cultures impact the supply chain in important ways. We found some indications of deliberate stockpiling by companies, for example. The head of the central medical stores of three out of the seven countries we initially approached for one survey were jailed or suspended from duty pending investigations of irregularities. Reported irregularities in public procurement are common; some of them are related to corruption. However, it is also worth noting that accusations of irregularities in procurement may be used as a political or an economic weapon. Rival politicians may seek to discredit an individual or party charged with procurement. Suppliers who do not win large public contracts have been known to allege corruption in order to freeze awards, leaving the market open to non-winners.

Where corruption or mismanagement are indeed in play, shortages may arise in some sectors even when upstream supply of products is assured. These effects can ripple through the market for many procurement cycles, adding layers of scrutiny or other additional red tape that outlive the risk and obstruct the flow of products.

*Lesson: Technocratic solutions to supply chain threats are unlikely to work unless they also take into account the political and institutional landscape.*

### **The market matters**

Politics are important, but so are market factors. Efforts to move towards the holy grail of "universal health coverage" mean that governments in middle- and some low-income countries are shouldering an increasing proportion of the bill for essential medicines. This broadly has the effect of driving down prices. Pressured to deliver medicines at lower prices, profit-seeking producers seek to cut costs, in part by "optimising" every stage of production and delivery. This in part accounts for the current concentration of production of small molecule generics in a small number of low-cost areas.

At the same time, most companies will look for opportunities to maintain and, where possible, increase their revenue—sometimes by increasing volume but often by raising prices. Producers and distributors routinely take advantage of secretive procurement

practices to achieve the highest possible price from each buyer. Previous research carried out by the Center for Global Development suggests that, as a result of this opacity as well as because of limited purchasing and thus bargaining power, and because of higher perceived risk of non-payment, low- and middle-income countries often pay more for essential medicines than richer countries do. Times of great uncertainty such as the COVID-19 pandemic provide additional opportunities to push prices up. Some price rises will be the result of real scarcity—a doubling of air freight prices and 60 percent increase in container shipment costs reported by Indian exporters is a case in point. Others may be the result of speculative manipulation of supply and/or opportunistic pricing.

To some extent, medicine markets are segmented by epidemiology, with some products, for example for infectious diseases common in the tropics, more in demand in lower-income countries and others, for example for chronic conditions associated with aging, consumed more in industrialised countries with older age structures. COVID-19 reminded us that where many buyers are competing for the same products, shipments to the highest payer may increase at the expense of patients in lower-income settings. As more countries progress through the epidemiological transition, this competition for similar products is likely to grow, with implications for the relative risk of shortages. Public procurement systems should of course strive for fair prices for quality-assured products. However, when supplies are constrained, suppliers will usually favour higher payers. Countries which focus largely on achieving the lowest prices in public procurement thus put themselves at risk; at the very least, flexibilities must be built in to procurement law to allow for rapid response in times of crisis.

*Lesson: Profit-seeking, including surge pricing and speculation, cascade through the supply chain, ultimately benefiting buyers who are least price sensitive.*

### **Global shocks may have local solutions**

Several of our analyses underlined the diversity of medicine availability in different markets at similar times. This was true even for molecules that were subject to a total export ban from India, including in markets to which India exports a lot. Central medical stores, wholesalers, and distributors reported different products out of stock in different countries, and the variation also held between wholesalers/distributors in a single country. At the retail level, there was limited correlation in reduction in sales of a particular product across different markets. This suggests that any supply disruptions detected at the global level do not cascade evenly through the supply chain.

Particularly severe and long-lasting deficits in supply—for example those caused by withdrawal of producers from the market because a product is not profitable—will be felt in many countries and across health sectors, and may best be solved by global efforts such as market-making through pooling of demand internationally, or new models for financing research and development.

However, in the case of sharper supply shocks, local factors such as rigid procurement regulations or poor fiscal planning can play a major role in determining which markets or

sectors will be left short of products and which will not. In follow-up interviews related to the central medical stores survey, various strategies to pre-empt or resolve shortages were described, many of them related to local procurement cycles or terms of payment. Common among the reasons given by wholesalers/distributors for stock-outs was limited access to credit or foreign exchange. These constraints relate to supply shocks tangentially or not at all; broadly speaking, they are local problems with local solutions. That said, global or regional efforts can help to create or support the infrastructures that allow for local solutions to emerge or be applied.

*Lesson: Supply shocks, even when global, only affect patients if they translate into shortages in local markets. Local solutions are often needed to manage global shocks.*

We also observed that many of our analyses were constrained by data availability and quality. This was in part because we were trying to spot patterns between countries. This is, of course, of interest when investigating how shocks to the supply of products at the highest level in a concentrated supply chain cascade down through the chain, and when trying to develop global early warning systems. From the point of view of individual countries wishing to avoid shortages of medicines needed by their patients, on the other hand, it is less important. In fact, many countries could access granular data that they could use to monitor looming shortages in their own market (see the discussion of data, below).

Within our study, we noticed anomalies between different data sources, and sometimes even from a single data source, suggesting that there may be unacknowledged resilience in the system. For example, several wholesalers and distributors reported shortages, even though a careful analysis of their stock levels suggested availability in excess of projected needs.

*Lesson: Better use of immediately available data, including more accurate demand planning, could in itself mitigate the risk of shortages.*

## **4. Implications of the learning exercise**

A great deal has already been written about the relationship between medicine supply and the risk of shortages. Some of the most commonly identified causes of drug shortages include complexities in the manufacturing processes (especially sterile manufacturing), demand uncertainties, regulatory actions, and supplier market exit due to low profit margins (WHO 2016, IMS Institute 2011, GAO 2014, Gray & Manasse 2011, Fox et al. 2014, Conti 2011, Woodcock and Wosinska 2013, Bogaert et al. 2015, Pauwels 2014). A number of strategies have been proposed to prevent drug shortages (Tucker et al. 2019, Gray 2014, WHO 2016), which include requiring purchasers and pharmaceutical companies to build redundancies, mandating that purchasers and procurers use failure-to-supply clauses, improving manufacturing and regulatory processes, and expanding and improving information sharing and reporting systems. There is also a vast body of literature on supply chain disruptions that provides operational details on sourcing contracts to mitigate supply disruption risks (see Pournader et al. 2020 for a recent review of such literature).

Here, we wish simply to summarise some of the questions that our work raises in the context of that body of work. We hope this section will provoke debate among governments and institutions interested in supporting sustainable access to quality-assured essential medicines, beyond the handful of programme medicines that have been of particular interest to international funders of health programmes in low- and middle-income countries.

### **Data: Its sharing, analysis, and use**

Buyers can't react quickly to a potential supply shock if they don't know where a product and its ingredients are made. And yet the pharmaceutical market is unusually opaque. Outsourcing is common; few regulators require market authorisation holders to state the location of manufacturing, and fewer still publish information on sources of active ingredients or excipients. Information sharing around production, procurement, and distribution of COVID-19 vaccines has demonstrated what is possible when the political will exists, although even in that case price data is kept under wraps by many countries. When it comes to essential medicines, tender results are not always published even in the public sector, and for on-patent products secret price negotiations are rife. In the private sector, undisclosed discounts are the norm. This lack of transparency creates scarcity and information asymmetry, creating a market for data on pharmaceutical production and sales. Add the high cost of collecting, cleaning, and standardising data to maximise its utility, and pharmaceutical market data become expensive to access, including for those who wish to use it to increase the efficiency of public procurement or for other "public good" uses not primarily intended to increase profit or competitive advantage.

Pharmaceutical manufacturers argue that sharing information about where they buy their ingredients and make their products would disadvantage them relative to their competitors. Most regulators derive their income from fees charged to pharmaceutical manufacturers, and appear to accept this argument from their clients, although it is hard to follow the logic of comparative disadvantage vis-à-vis competitors who would equally be required to share the same information.

In an increasing number of markets with consolidated national procurement, the buyer potentially has the power to compel bidders to be more transparent about the source of their medicines, in a similar way that Turkey obliged manufacturers to invest in systems allowing for end-to-end track and trace for all medicines reimbursed by the national insurer. The WHO requires manufacturers who wish to prequalify their products as quality-assured to disclose sources of active ingredients, though the programme is currently limited to a handful of programme products. Some national regulators (of both medicines and markets) also overrule the protestations of lobbyists and require companies to disclose the source of medicines; PHARMAC in New Zealand is an example. The sky has not fallen and the New Zealand market remains well-stocked with medicines. Most, however, do not even ask companies for information that could help monitor levels of production or consumption, nor do they analyse customs and excise data which could provide granular information on trade, and thus help monitor risks of shortages.

An important step in helping protect against medicine shortages at the national level, where most shortages occur and must be resolved, could be to support countries in making better use of the data they already have, which at the very least provides information on the country from which finished products or active ingredients are imported. A further step could entail supporting a global effort to requiring greater disclosure of the origins of registered products, active ingredients, and excipients.

Our team had exceptional access to a variety of proprietary data sets that were relatively well-structured, and Maisha Meds also invested significant time in cleaning less structured trade data. Despite this, we were not able reliably to correlate signals of supply disruption with specific shortages. From this we conclude that, given the data currently available, there is unlikely to be a tidy, tech-driven solution to spotting or pre-empting impending shortages of most non-programme essential medicines in specific countries using internationally available trade and market data alone.

However, both Maisha Meds and IQVIA developed prototype predictor models that could be further refined. Collecting data that would allow for models to be trained on data relating specifically to shortages in middle- and in lower-income markets would be valuable in this process. Because supply chains are long, and products take time to flow through them, models might also perform better at predicting shortage outcomes over a period longer than the three- or four-month window used in our initial analyses of COVID-19-related shocks.

Data quality challenges might be reduced by the development of agreed FAIR-compliant data standards/ontologies for pharmaceutical production, market, and trade data. Public investment would be needed to integrate these ontologies into existing trade reporting mechanisms so that they reduce, rather than multiply, the burden of reporting. Though machine learning cannot fill data gaps, investment in developing and training machine learning models could help to clean and standardise existing data format for analysis.

### **Questions raised**

What is the "minimum ideal" dataset for predicting shortages of a specific product in national markets? If these data were available to national regulators, would they use it proactively to signal potential shortages in the supply chain? Who would lead the fight for greater transparency, which will be opposed by R&D and generic pharma alike?

What are the incentives and, especially, disincentives to standardise data on national production, consumption, imports, and exports of specific products, and share them through an internationally accessible platform? Is it politically feasible to share data internationally? What problems might internationally standardised data solve at the country level, that can't be solved with data already or potentially available locally? Whose job is it to do that analysis and solve those problems?

Who would have to do the work of generating standardised data, and who would pay them? How much would it cost, and what are the likely benefits in terms of reduced shortages caused by supply shocks, taking into account all the other causes of shortages?

## **National demand forecasting and procurement**

While our investigation focused on supply shocks, procurement practices—which shape the demand side—also have an important role in mitigating the risks of shocks to supply, by allowing suppliers to plan adequate production in the first place.

Currently, some countries base their public sector demand forecasts on historical data (much as our models were trained on historical trends). However, these forecasts do not take into account known deviations from normal volumes, unlike the IQVIA Shortage Detection Model, which was specifically trained on data relating to known anomalies (shortages). This means that previous shortages can get carried through into new low-demand forecasts, leading to under-procurement and continuing chronic shortages. Extending the discussion about better use of data at the national level, more accurate demand forecasting, and support for procurement practices that signal that demand to the market in good time, may help to ensure that producers at least plan to produce in quantities adequate to meet real demand.

### **Questions raised**

Our study did not look specifically at national demand planning, only at prevalent and expected shortages in central medical stores. The first question must therefore be: Is there evidence that shortages result from routine underestimation of medicine volumes, rather than unfulfilled orders? If yes, would technical support for demand planning for essential (non-programme) medicines improve the situation? What would it cost? What are the incentives and disincentives for countries to plan demand and procure medicines more efficiently? To what extent is procurement constrained by limited budgets rather than poor demand planning?

## **Global products, local patients**

Many of the current vulnerabilities in the supply chain derive from the mismatch between optimised production and generalised need. Production (for each part of the supply chain— APIs, excipients, packaging, finished products) is concentrated in specific geographic and political locations, often far from the centres of need, which are spread across the globe.

Three suggestions for reducing the mismatch between globalised production and local consumption emerged from our analysis.

### **1. Increase redundancy**

The pharma industry maintains its efficiency (and thus its profitability) by "optimising"—often outsourcing to low-cost producers, and minimising stock on hand as much as possible throughout the supply chain. The optimised model also centres on large batch production, which achieves economies of scale but reduces adaptability. Cost-cutting threatens quality, but it also reduces the ability to absorb any shocks in times of reduced supply or spikes in demand.

Studies examining markets for medicines and other commodities directly linked to COVID-19 suggest that when supply and demand shocks hit all countries simultaneously, prices will rise for reasons of scarcity or speculation. While these effects did not filter consistently through to the essential medicines we examined, there is some evidence, seen in the relative changes in export volumes from India by region, that the mere threat of shortages of essential medicines encourages richer clients to outbid those less able to pay. This leaves rich clients out of pocket, and poor clients out of stock.

One way to reduce the risks associated with dramatic supply shocks is to "de-optimize," in other words to increase redundancy in production capacity and stocks throughout the system so that spare capacity is available in times of crisis. Because this introduces inefficiency, it will increase the unit cost of production and storage. In consequence, producers and distributors will have to accept lower profits, or governments and other consumers will have to pay slightly higher prices, or both, all of the time. Countries that use their bargaining power well in procuring medicines (many of them wealthier countries with near-universal health coverage) now pay very low prices for most essential medicines most of the time, and high prices only in times of crisis. To those who can afford the surge pricing, this market model may be preferable to one in which increased redundancy raises prices for everyone, all the time, in an effort to ensure supplies to poorer clients in times of crisis.

### *Questions raised*

How much would increased redundancy for essential medicines add to unit cost of production and storage? Who will foot the bill? If prices rose as a result of increasing buffers to protect against supply shocks, might that effectively reduce access for the poorest countries and patients all of the time? If yes, could that outweigh any gains that result from a buffer for times of crisis? What hedging or other mechanisms might spread the cost of redundancy?

## **2. "Globalise" the market**

Another way of achieving more balance between a global supply chain and local consumption is to aggregate purchasing at a supra-national level (for example regional or global), through pooled procurement. While nothing in our analysis points directly to pooled procurement as an effective protection against supply shocks, the possibility was raised in several earlier meetings in which our preliminary findings were presented.

Pooled procurement mechanisms are much talked about but little implemented, other than for commodities of particular interest to global health funders. There are currently very few well-functioning intercountry pooled procurement mechanisms that buy a wide range of essential medicines procured principally by national governments. The Pan-American Health Organization negotiates group purchases for some essential medicines for country governments, who pay through the Strategic Fund. Among country-led mechanisms, those that do currently operate well, such as that run by the Organisation of Eastern Caribbean States (O ECS), tend to group countries that have no ambitions in terms of developing local

industry, share very similar characteristics in terms of market size and epidemiological need, and have existing financial arrangements (a shared currency and central bank) that facilitate sustainable payment mechanisms. Attempts to establish mechanisms in the African region are longstanding. The Southern African Development Community has been talking about pooled procurement since 1997, and the East African Community since 2006; neither has yet bought a single pill through a pooled mechanism.

The Africa Medical Supplies Platform (AMSP), set up to facilitate procurement of COVID-19-related commodities for African Union member states, potentially provides a new model for price transparency and demand aggregation in the African continent. In its current form it is an institutionally endorsed e-commerce platform with a restricted buyer pool and, reportedly, quality assurance for items on offer. This differs from the better-established pooled procurement mechanisms (such as the OECS pooled procurement service or the Global Drug Facility for TB medicines) in that it apparently provides minimal support for demand planning, buffer stock management, product registration, the provision of contractual certainty or legal recourse. In its terms and conditions, AMSP specifically disavows any role in procurement of goods (see <https://amsp.africa/terms-conditions/#>). In addition, many countries would be prohibited by national procurement regulations from buying from the platform, were it not for the waiving of provisions in response to the COVID-19 emergency. However, AMSP's online platform already offers a wide variety of medicines, from acne cream and gripe water to artemisinin combination therapy and statins. Given the political support for the platform and its rapid deployment, AMSP may provide a well-branded base upon which a more sustainable and transparent procurement system may be built over time.

### *Questions raised*

Why have existing attempts to establish multi-country pooled procurement of a wide range of essential medicines in sub-Saharan Africa not made more progress? Could the current efforts be replaced by e-commerce platforms that drive buyers to a limited number of quality-assured providers while providing price transparency? Who will pay for quality assurance? What governance structures would be necessary to ensure that contracts are honoured, including in times of heightened demand?

Who will support the regulatory harmonisation needed to make any pooled procurement model work outside of emergency situations? Is there any appetite among global health funders to support a third-party platform which provides the services currently associated with successful pooled procurement (such as demand planning services, maintenance of a rotating fund, and buffer stocks) for essential medicines not currently covered by global programmes? How much would it cost and who would pay?

Could an externally sponsored platform override national procurement regulations for medicines commonly bought by governments? What are the incentives and disincentives for governments to share control of their regulatory process with other countries through harmonisation? What are the incentives and disincentives for governments to entrust procurement of essential medicines to a third party?

### 3. Localise production

Most low-income countries are heavily dependent on imported medicines; Indian generics made from Chinese active ingredients dominate many markets in sub-Saharan Africa, for example. Diversifying sources of supply spreads the risk, so that if supply from one source dries up—perhaps because of an industrial accident, natural disaster, or trade dispute—other sources are available.

In fact, even the clear supply shocks of COVID-19 do not appear to have led to a crisis of availability of essential medicines in many of the study countries, at least in the short term. However, the logic of diversification of medicine sources remains strong, especially if the alternative sources are at least as likely to provide quality products at similar prices, and if the risk of disruption from those alternative sources are slight.

Analysis undertaken in this project suggests that increasing production of solid formulations within sub-Saharan Africa could contribute to security of supply for producing (and perhaps also importing) countries in the region in the longer term. Since production in all countries is not feasible, this presupposes that some countries will source some of their imports from other countries in the region, rather than from Asia, as is currently common.

The proposed spoke-and-hub model, with initial hubs sited in a handful of areas with good existing infrastructure and transport links, implies co-production within an international network. To succeed, that would require high levels of cooperation on quality assurance, market authorisation and other issues of medicine and excise regulation between countries within the network, and between network countries and importers.

No countries in the region other than South Africa currently produce APIs in any quantity, and capital constraints mean that stocks of imported API held locally are generally lower than in producing countries in Asia, meaning that risks to local production of any disruption to supply of APIs is considerable. However, our analysis deemed it unlikely that API production would be cost-effective in the medium term, so increasing production of finished products in sub-Saharan Africa would not diminish the upstream risk to supply.

#### *Questions raised*

How feasible is it to harmonise trade, customs, quality, and market regulations in support of the goal of more production in those sub-Saharan African countries where infrastructure is already relatively well established? How would this affect the unit cost of medicines? Will importing from other sub-Saharan African countries increase security of supply in those countries not involved in the final production of finished medicines? What is the opportunity cost of this strategy? What are the likely sources of capital needed to implement the strategy?

## **Conclusion**

These many questions bring us to the unsurprising but inevitable conclusion that "it's complicated." There are unlikely to be easy technical fixes to shortages that arise from political as well as economic imperatives, particularly when those imperatives include a desire to maximise access to quality-assured essential medicines nationally on the part of many governments, and the simultaneous desire to maximise profits globally on the part of many producers and distributors.

Addressing the continuing problem of medicine shortages, and in particular those caused by shocks to a supply chain concentrated to minimise production costs, will require important trade-offs. The price of greater security in pharmaceutical supply chains may well be more expensive medicines. Someone will have to pay the price; there is a risk that it will be the governments or citizens least able to pay, either because they have to spend more for their medicines, or because they are priced out of the market and can't afford to buy them at all. The challenge for global health organisations is to find politically acceptable ways to ensure that doesn't happen, while also avoiding any increase in dependency on ultimately unsustainable external funding.

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## Appendix

Table 1. Medicine included in this study

Key	Market-wide data	India export data	Wholesaler panel data	Product registration and disruption data
Acyclovir—oral solid	✓	✓	✓	✓
Allopurinol—oral solid	✓		✓	✓
Amikacin—parenteral	✓	✓		✓
Amiodarone—oral solid	✓	✓		✓
Amitriptyline—oral solid	✓		✓	✓
Amlodipine telmisartan—oral solid	✓	✓	✓	✓
Amphotericin b—parenteral	✓			✓
Azathioprine—oral solid	✓	✓		✓
Beclomethasone—inhaled	✓	✓		✓
Betamethasone	✓		✓	✓
Budesonide	✓		✓	✓
Bupivacaine	✓		✓	✓
Calcium folinate—parenteral	✓			✓
Carbamazepine—oral liquid	✓	✓	✓	✓
Cefotaxime	✓		✓	✓
Ceftriaxone—parenteral	✓		✓	✓
Ciprofloxacin—oral solid	✓	✓	✓	✓
Cloxacillin—oral liquid	✓		✓	✓
Dapsone—oral solid	✓			✓
Dexamethasone—parenteral	✓	✓		✓
Digoxin—oral solid	✓	✓		✓
Doxycycline—oral solid	✓		✓	✓
Enalapril—oral solid	✓	✓		✓
Fluconazole	✓		✓	✓
Fluoxetine—oral solid	✓	✓	✓	✓
Gentamicin	✓		✓	✓
Hydralazine—oral solid	✓			✓
Hydralazine—parenteral	✓			✓
Hydrochlorothiazide—oral solid	✓	✓	✓	✓
Hydrocortisone—topical	✓			✓
Ibuprofen—oral solid	✓		✓	✓
Levonorgestrel/ethinylestradiol	✓		✓	✓
Lisinopril	✓		✓	✓

Meropenem—parenteral	✓	✓	✓	✓
Methylprednisolone—parenteral	✓	✓		✓
Metoclopramide—oral solid	✓	✓		✓
Metronidazole	✓		✓	✓
Metronidazole—oral liquid	✓		✓	✓
Mifepristone misoprostol—oral solid	✓		✓	✓
Morphine—parenteral	✓			✓
Mupirocin—topical	✓	✓		✓
Naloxone—parenteral	✓			✓
Nevirapine	✓		✓	✓
Norethisterone	✓		✓	✓
Omeprazole—oral solid	✓	✓	✓	✓
Oxytocin—parenteral	✓	✓		✓
Paclitaxel	✓		✓	✓
Paracetamol—oral solid	✓		✓	✓
Phenobarbital—parenteral	✓			✓
Prednisolone—ophthalmic	✓		✓	✓
Pyridostigmine—oral solid	✓	✓		✓
Ranitidine—oral solid	✓	✓	✓	✓
Rifampicin—oral solid	✓			✓
Salbutamol	✓		✓	✓
Sofosbuvir	✓		✓	✓
Sofosbuvir/velpatasvir	✓		✓	✓
Spirolactone—oral solid	✓	✓		✓
Sulfadiazine—topical	✓	✓		✓
Sulfamethoxazole trimethoprim—oral solid	✓		✓	✓
Telmisartan	✓		✓	✓
Tetracycline	✓		✓	✓
Valproic acid—oral liquid	✓	✓		✓
Vitamin a/retinol—oral solid	✓		✓	✓
Vitamin b complex	✓		✓	✓

**Table 2. Analysis undertaken in each country**

Country	India export data	Pharmacy data	Market-wide data	CMS survey	Wholesaler survey
Bangladesh			✓		
Benin			✓		✓*
Burkina Faso			✓		✓*
Cameroon			✓		✓*
Chad			✓		✓*
Congo			✓		✓*
Gabon			✓		✓*
Gambia				✓	
Ghana		✓			✓
Guinea			✓		✓*
India	✓	✓			
Indonesia			✓		
Côte d'Ivoire			✓		✓*
Jordan			✓		✓
Kenya	✓	✓	✓		✓
Lebanon			✓		
Malawi				✓	
Niger			✓		✓*
Nigeria		✓		✓	✓
Pakistan			✓		✓
Senegal			✓	✓	✓*
Togo			✓		✓*
Turkey			✓		

✓\* countries were included as part of a Francophone West-African wide survey