

Dependence on India

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1.0 Introduction

Pharmaceutical supply chains can be long with manufacturing of active pharmaceutical ingredient (API), excipients, packaging and finished formulation being carried out in different countries. At the same time certain countries, notably India and China, have come to dominate the production of active pharmaceutical ingredient and finished products, particularly for generic medicines. This paper describes different attempts to determine the extent to which certain low and middle income countries are dependent on India for the selected set of essential medicines. It forms part of a wider collaborative effort between CGD, IQVIA and Maisha Meds aimed at understanding how COVID-19 has impacted supply chains for vital medicines, including countries' reliance on India for their essential medicines. The latter is important because over reliance on one region or country for drug production can leave buyers more vulnerable to shocks, such as the closing of factories, disruption of trade or export bans all of which we have seen with the Covid crisis. Between 70 per cent and 90 percent of drugs in Sub-Saharan Africa are imported, making the region the most import dependent of the developing world. India is the world's largest supplier of generic drugs, and also supplies much of the programmatic commodities for HIV, TB and malaria to the continent, so this trading relationship is of particular interest.

2.0 Background

Products are sold in countries by Marketing Authorisation Holders, or in other words, the company that is responsible for the sale, distribution and monitoring the safety of that product. The Marketing Authorisation Holder need not be the manufacturer, for example where it sells the product under license from another organisation, and the corporate headquarters of the Marketing Authorisation Holder need not be in the country where the products are manufactured or sold. The identity of the Marketing Authorisation Holder thus holds few clues to the manufacturing site, or the source of the API.

Countries' trade flows in pharmaceuticals can be described in broad terms from import and export databases such as UN COMTRADE. However, these databases contain information only at an aggregate level, with very little insight into which group of products lie behind the numbers. Often very different types of medicine and are included in the same six digit code, sometimes alongside non-medical produce such as plastics. The usefulness varies by the type of code, insulin have their own six digit number, whilst antibiotics are all combined together. Thus one can see the value of antibiotics exported by a country, but not which antibiotics. Similarly as unit quantities are provided in multiple formats in the source databases, and KG weights can include the weight of the box or outer packaging quantities, even in aggregate, are unreliable. Moreover, these trade flows do not necessarily describe the full voyage taken by a pharmaceutical. Some products made in India but destined for Francophone Africa will be shipped to France before making their way onward to countries like Senegal, Cameroon, Togo and the like. Manufacturers also operate distribution hubs bringing products by air or sea into single locations like in Switzerland or Kenya, for supply to other

countries. These re-exports or onward exports are not well captured in the import and export databases, even in aggregate.

India is one of a small number of countries (including Canada, Indonesia, Australia, Denmark) that releases its export data at line level, giving some information at least on the product that is exported and the value of the shipment, as well as its destination. In the following paragraphs we describe our attempts to use these data, in combination with other data sources, to estimate a country's reliance on India for finished product, in terms of volume, in 2019.

In this study we evaluate (i) the feasibility of using Indian export data to estimate total volumes of selected medicines exported from India to a specific set of countries; (ii) the feasibility of extrapolating usage data from other low and middle income countries to estimate likely ranges of usage of a specific set of essential medicines in countries for which no data are available. By doing this we look to estimate a country's reliance on India by comparing exports from India with estimates of total usage.

3.0 Methods and data sources

3.1 Country and product selection: The countries selected for this study were Bangladesh, Indonesia, Jordan, Kenya, Lebanon, Turkey and 12 countries in Francophone Africa (Benin, Burkina Faso, Chad, Cameroon, Congo, Cote d'Ivoire, Gabon, Guinea, Mali, Niger, Senegal, Togo). These were chosen because they are LMICs aligned with priority geographies of development partners, and for which some information on private sector volumes by product were available from IQVIA. Products selected for this study are described in Table 1. Twenty one of these molecules+forms were selected on the basis of the following criteria (i) sold through the private sector in most of the selected countries, (ii) apparently dependent on India in at one other country of interest to development partners (Ghana) and (iii) categorised as both Vital Essential Medicines in two national Essential Medicine Lists and an Essential Medicine by the WHO. The remaining three products were added from the current WHO Essential Medicine, and List and chosen so as to ensure an adequate representation across product forms and therapy classes.

Table 1: Selected Molecule+Forms

Molecule + Form				
ACICLOVIR ORAL SOLID	BECLOMETASONE INHALED	DIGOXIN ORAL SOLID	METHYLPREDNISOLONE PARENTERAL	PYRIDOSTIGMINE ORAL SOLID
AMIKACIN PARENTERAL	CARBAMAZEPINE ORAL LIQUID	ENALAPRIL ORAL SOLID	METOCLOPRAMIDE ORAL SOLID	RANITIDINE ORAL SOLID
AMIODARONE ORAL SOLID	CARBAMAZEPINE ORAL SOLID	FLUOXETINE ORAL SOLID	MUPIROCIN TOPICAL	SPIRONOLACTONE ORAL SOLID
AMLODIPINE#TELMISARTAN ORAL SOLID	CIPROFLOXACIN ORAL SOLID	HYDROCHLOROTHIAZIDE ORAL SOLID	OMEPRAZOLE ORAL SOLID	SULFADIAZINE TOPICAL
AZATHIOPRINE ORAL SOLID	DEXAMETHASONE PARENTERAL	MEROPENEM PARENTERAL	OXYTOCIN PARENTERAL	VALPROIC ACID ORAL LIQUID

3.2 Volume of Indian exports: To estimate a country's reliance on India, the volume of Indian exports and the total usage of that product in that country need to be known. On the former, Indian export data are made available by a number of different vendors. Such data may include information by molecule or by brand, or both. Text searches, including text searches designed to identify common mis-spellings of molecule or brand name, were used to link export data to the products of interest.

3.3 Estimating total volume of specific molecule+form: To estimate dependency on India, total volumes for each of the selected molecule+forms are required. In most low and middle income countries, public sector purchases of the selected medicines are not made publicly available. As such even though private sector volumes may be available, and are for the selected countries, total

volumes are not. In order to estimate total volumes in our selected countries, and in most low and middle income countries, alternatives need to be devised. In this study an attempt was therefore made to investigate the possibility of estimating total volume using ranges calculated from data collected in other low and middle income countries where IQVIA has complete coverage of both public and private sectors. This would make the assumption that low and middle income countries are, to some extent at least, similar in terms of their usage of essential medicines, allowing for differences in population and/or epidemiology. In this study, therefore, the following data were therefore combined to produce estimates indicating the likely range that would describe usage of the selected medicines in the countries of interest; (i) volume data extracted from 15 other middle income countries where IQVIA has data from both public and private sectors; (ii) prescription data from more than 30 high, low- and middle- income countries where IQVIA collects information, this being used to determine the most common diagnosis for which the selected molecules+forms were prescribed, and (iii) information on prevalence and incidence for those diseases for which those molecules were most commonly prescribed, as extracted from the Global Burden of Disease Study 2018 (<http://ghdx.healthdata.org/gbd-results-tool>).

To calculate a range describing likely total usage of each molecule+form in a low or middle income country, total volume as estimated from IQVIA's databases in each of the 15 countries was divided either by population and, as an alternative, by the number of prevalent or incident patients (as appropriate) with the disease for which the molecule+form is most commonly prescribed. Total volume was expressed in IQVIA's standard units. Volume was thus expressed in terms of number of tablets, number of vials, number of doses of inhaled medications or number of grams of cream or ointment, as appropriate.

3.2 Volume of Kenya imports: To estimate a country's reliance on India, an alternative methodology is to look at the Import data from the recipient country. This project was able to obtain Kenyan import data for 2019 from a vendor. In a similar manner to the Indian exports the data was searched for text strings by brand and molecule. Import dependency was calculated as a % of import value.

While this methodology is effective in identifying Indian import dependency it is not without its own issues. The quality and completeness of import data is often quite poor. As such is it more difficult to build a volume estimate by product, as done in the instance of the Indian export data. Furthermore, it is not advisable to project from one country's import dependence to others in the region, unless this is corroborated through other sources, such as registration records.

In theory another good use of this data would be to validate shipments from India to their country destination. However, it is nigh on impossible to do this consistently, and if you manage to link some parts of the information, you can find that the Indian export value is higher than the country import value. This may be because there are/were incentives in place that encourage values in Indian exports to be high (a 5% tax rebate from the Indian government), and there may be incentives to reduce reported import values (as taxes and duties are priced as a % of the import value).

3.4 Validating the results: IQVIA's private sector volume data was used to help validate results. In countries deemed dependent on India for a particular molecule+form, for example, the volume of Indian exports should be multiples of the volumes seen in IQVIA's private sector data. On the other hand, where India was not deemed to be an important supplier, we would expect to find that volumes in IQVIA's private sector data might be larger than those seen in Indian exports, or at least a major component of those Indian exports.

4.0 Results

This section is divided into two parts: (i) We evaluate the feasibility of using Indian export data to estimate total volumes exported from India, and (ii) We evaluate the feasibility of extrapolating usage data from one set of countries to others within a similar income category.

4.1 Evaluating the feasibility of using Indian export data to estimate total volumes exported from India to specific countries: Estimating the total volume of Indian exports proved challenging. For many countries there was insufficient information to identify the pack size precisely (Table 2 shows the percentages of lines with incomplete data by country). Data relating to quantities are also suspect in several cases, with the units of measure not being specified or being incorrect. In the absence of such data, it is impossible to estimate volumes exported by India to a specific country reliably. The extent of error can be minimised by using the information from those lines where information is complete to estimate an average price per unit, and dividing the value of other shipments by this average price to estimate their volume. Nonetheless it is evident that prices per unit are not normally distributed and that as such the median price and average price can often be different. It should also be noted that shipment date is not the same as usage date. Products may not be manufactured throughout the year, and manufacturers may wish, and encourage, sales of large quantities that are destined to be used for up to and more than one year from the date of shipment

Table 2: Number of shipments for all molecules+forms, and % with insufficient information to identify pack size precisely where assumptions had to be made

Countries	Total Shipping	Assumption Scale
Benin	184	91.8%
Guinea	101	88.1%
Cameroon	90	75.6%
Mali	62	64.5%
Chad	49	73.5%
Senegal	47	89.4%
Ivory Coast	44	86.4%
Niger	30	80.0%
Burkina Faso	27	74.1%
Togo	24	83.3%
Gabon	0	0.0%
Congo	0	0.0%

Countries	Total Shipping	Assumption Scale
Kenya	312	56.4%
Turkey	69	75.4%
Jordan	31	48.4%
Lebanon	30	73.3%
Pakistan	12	66.7%
Bangladesh	2	100.0%
Indonesia	0	0.0%

4.2 Estimating the likely range of total usage from other countries' data: As noted above, an attempt was made to estimate total usage in countries without data from a set of other middle income countries where total usage data was available. The other countries's data was used to describe a range of usage for each molecule+form. To extrapolate these data to another country however, such a range is only useful if it is relatively small or at least consistent. To gauge the utility of the ranges calculated, the "interquartile range: median" ratio was calculated. The lower the "interquartile range: median" ratio then the more similar countries are in terms of the volumes of the product used. Table 3 shows the "interquartile range: median" ratio for the products selected. This table demonstrates that use of the majority of products varied considerably across countries. As an example, the median volume per capita across 15 countries for enalapril was 3.1 standard units per year, whilst the first quartile value was 0.5 standard units per capita and the third quartile was 9.1. This represents a very large spread of values and such variation in the volumes makes using this method to estimate volumes used in another country inherently unreliable.

Table 3: IQR to median ratio

IQR to Median ratio	Number
>2.5	4
>1.75 to <2.5	4
> 1 to <1.75	11
<1	6

4.3 Validation of the results: As described above attempts to estimate the volumes reported as being exported from India to a specific country, as well as to estimate total usage in each country proved unreliable. It was not therefore appropriate to compare volumes seen in the IQVIA retail data with those estimated from the Indian export data. However investigations did reveal that in several cases products were found in the retail data that did not appear to be exported from India in the same year. From this we might be tempted to assume that India is not a major supplier but as noted above India's exports may have been shipped in the previous calendar year, or may have been exported to a third country prior to shipment to its final destination.

5.0 Discussion and recommendations

In this paper we have attempted to use trade and sales data to assess a set of low and middle income countries dependence on India for supply of a subset of Vital Essential Medicines. We have focused on India because India has comparatively rich export data, and because India is a key exporter of pharmaceuticals.

However despite India releasing far more export data than most other countries, and our team having access to an extensive IQVIA wholesaler dataset, as well as prescription data, global burden of disease information and UN COMTRADE data, we have not been able to estimate the extent to which countries rely on India for their vital medicines. This is for two reasons - first the quality and completeness of Indian export data, whilst unique and of itself valuable, is not sufficient to provide reliable estimate of exports from India, and second because it has been shown that the likely levels of usage of VELs cannot be extrapolated from one country or group of countries to another.

- Understanding the source of products of essential medicines, however, is critical to designing more secure pharmaceutical supply chains for the following reasons. Enhance global health security/ensure uninterrupted supply: A lack of transparency in product origin and journey makes it impossible to protect against supply shocks such as those caused by the COVID-19 outbreak and to predict and mitigate shortages. It is much more difficult for purchasers and governments to insulate themselves against shocks when it is not clear who they are reliant on for their supply. Equally, convoluted and opaque supply chains mean suppliers cannot reliably predict demand patterns and [plan accordingly](#).
- Improve efficiency/reduce waste: On the procurement side, transparency will reduce information asymmetry, between purchasers and suppliers, making the market more efficient and competitive. If purchasers have good information on where products originate, their journey and, ideally, the terms by which goods are being imported and exported globally, the marketplace will become more competitive, trimming unnecessary mark ups and, if the manufacturer is known, improving visibility of medicine quality
- Improve care quality and health outcomes: Finally, from a health standpoint, making it easier to track a product, will give crucial medical and epidemiological information to country planners and regulators. This can make it easier to track illnesses, as well as areas where outdated treatments are still relied on, or if certain drugs are being over (or under)

prescribed. Such data can help in the fight against antimicrobial resistance. Utilisation data can offer signals about [illicit or falsified medicines](#).

1. HS code data at high frequency. We can insert into Ngozi' s agenda if she wins.

What next? A centralised cross national database: economies of scale and scope

- For smaller countries and low volume products, an approach that looks only at a single country import data is likely to miss important trends and potential shortages until it is too late. Trade data to individual countries is very choppy. I would argue that it is only by aggregating the data to a regional level is it possible to spot changes in time, though these high level trends would also need to be linked to in-country data.
- While national governments *can* analyse their import data to develop an understanding of the market they currently don't tend to, even if like Pete suggests they increasingly have the ability to do so. I can't think of a single country, except for Zambia and Uganda up to 2016 where IQVIA did the work, that actually systematically captures and cleans their import data. The PPB in Kenya was asking for a grant from the World Bank to do just this, but I don't think it was ever given.
- Using export data rather than import data can be much cheaper. Pete knows much more about this than I do, but the import databases for Zambia and Uganda cost something like \$100,000-200,000 to develop (I don't remember the exact figure sorry Pete but I remember the stories of a shipping container full of paper shipment manifests). An approach that used export data would benefit from processing all the data using a single algorithm and centralised expertise. In theory once set up it would be possible to provide ongoing data on all countries for not much more cost than processing data for a handful of countries individually.
- Export data is generally more complete, and we would also assume accurate, than the import records captured at the ports in Africa. Though this could be improved with specific effort by national governments this would add an extra step to the process.

I agree that we should be clear about who could actually use this information and for what. For the reasons above I do think there is a merit to doing this centrally, though countries would obviously need to be invested in the process as well to want to use the findings. I also agree that some countries will likely not appreciate the sudden transparency into their affairs.

Data could also be used for other things like health econometrics, transnational price comparisons and supporting investment in local manufacturing. However, I would prefer to keep the focus on medicine shortages for now.

6.0 Conclusions

This paper investigated the possibility of using a combination of Indian export data, IQVIA private sector sales data and IQVIA public sector and prescription audit data to assess a specific group of countries' dependence on India on exports of finished products country by country for a selection of African LMICs.

The analysis was complicated however by the lack of information contained on pack size in the Indian export data. It faced a further challenge when it was found that the use of the products being

studied varied considerably across 15 low and middle income countries where IQVIA has both public and private sector data, making extrapolation from one set of countries to another inherently unreliable.

India is unique amongst major pharmaceutical manufacturing hubs in making its export volumes available at line level. To understand a countries' dependence on any one of these manufacturing hubs requires more than just Indian export data, however, and more consistent and more complete data than is currently seen in the Indian export data files. Another option would be to make country import data or public sector data available, and several countries make these data available for particular purposes, although again, quality and completeness of the data can make interpretation as challenging as the Indian export data. In our view it is only when more accurate data can be gathered on public and private sector volumes, and regulators are willing or able to release information on site of manufacture for each product (as some already are), that a country's reliance on a particular country for pharmaceutical supplies will be able to be assessed.

Better data visibility will enhance countries' robustness, ie ability to respond to and function during a C19 type crisis and is in our opinion a global and domestic policy imperative at a time when introspection and nationalistic tendencies seem to be on the rise.