Those who do not move, do not notice their (supply) chains—inconvenient lessons from disruptions related to COVID-19

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An Italian comedian once joked:

“Americans buy thousands of tons of Danish cookies, and Danes buy thousands of tons of American cookies, with a coming and going of ships, airplanes, trains. Is this sensible? Maybe it is, because the cookies are different. But why wouldn’t they just swap recipes?”

The target of this joke is ‘competitive’ imports. These are commodities that an economy could, and indeed does, produce to some extent, and which the 2019 coronavirus (COVID-19) pandemic has raised concerns about in the context of national security and healthcare.

A double-whammy of supply disruption and unprecedented demand hit most healthcare systems. Firstly, the lockdown exposed the extent to which the supply of medicines depends on a handful of locations. An example is the global reliance on China for the manufacture of APIs – active pharmaceutical ingredients (Anonymous 2020).

Secondly, the rapid escalation of severe and critical cases is a reminder that the resources available to hospitals and labs are limited. An example is the intensification of COVID-19 testing campaigns. Indirectly, this caused abnormal demand for reagents to extract the virus’ nucleic acid from samples—in short: RNA extraction kits (Mehta 2020).

Most countries could not meet this demand in the absence of a home-grown manufacturing base (Smyth et al. 2020).

The examples above are not about glamorous, ‘high value’ items. Yet they caused national security-level distress. In hindsight, it is easy to draw conclusions. At exceptional times, we wonder why everything is not on hand in our backyard—even the cheapest face mask, lab reagent, and API. At any other time, we wonder why medicines are pricey, and why healthcare spending is not in check.

It is tempting to look for definitive answers about the risk of depending on a foreign manufacturing base. But is it reasonable to assume that a 100% homegrown healthcare supply is possible? Is it reasonable to expect ‘always on’ readiness end-to-end—from manufacturing to the patient, in both normal and exceptional operating conditions? At the least, no one has figured it out yet.

Instead, I offer a few, inconvenient lessons we might consider learning. Roughly, these can be grouped into three topic areas: (1) Choosing sourcing locations. (2) Establishing supply dependencies through outsourcing and offshoring decisions. (3) Matching supply to a changing, often erratic demand.

The reminder is loosely based on previous work on pharmaceutical supply risk carried out within a recently concluded collaborative research project on Reconfiguring Medicines End-to-end Supply—ReMediES (Geyman et al. 2020).

1 Choosing sourcing locations

Obviously, there are textbook reasons to manufacture off-shore. These include foreign market penetration and cost containment—typically labour (see e.g., Dornier et al. 1998: p. 258). Outsourcing, foreign direct investment and other mechanisms support these classic location strategies—at least until other developments undermine their benefits. In 2017, a hurricane gave the finishing blow to the already fragile economy of Puerto Rico. Until then, tax breaks had secured the presence of major pharmaceutical manufacturers for decades (Smith 2019). In this case, too, medicines supply felt the hit, all the way to patient care (Barrera et al. 2018).

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1 Freely translated from the Italian. Source: p 240; Grillo B (2006) Tutto il grillo che conta: Dodici anni di monologhi, polemiche, censure. Feltrinelli, Milano.
So, what other factors determine a good manufacturing location?

Lesson 1: The pandemic started where it was supposed to start. As Silver (2013: Ch.7) points out, influenza virus epidemics are recurrent events. Repeatedly, their diffusion behaviour eludes predictions and baffles decision-makers. Yet, they do not come out of the blue. Before becoming global pandemics, dangerous viral flu strains originate in conditions that are relatively easy to identify. According to Silver, these include the following: (1) A diet in which pig is a staple. (2) Geographical conditions for pigs and seafaring birds to intermingle. (3) Areas with poor hygiene and sanitation conditions, that help the transmission of animal viruses to humans. Countries like China check all the boxes above. From the viewpoint of facility location or sourcing decision, this is good to know. Except these countries also enjoy ‘textbook’ comparative advantages as manufacturing locations.

Lesson 2: Location-specific issues can be a challenge for back-of-the-envelope calculations. Reasons for ‘vetting’ specific locations go beyond extreme, albeit recurring, events like pandemics and hurricanes. Even before COVID-19, the dependability of Chinese and Indian API manufacturers was low. In 69% of cases, an adverse regulatory inspection could result in a medicines shortage up to four years later (Geyman et al. 2020). In principle, getting more insights can shift future location decisions.

But this depends on which objectives a supply chain is designed to achieve. Not long before the pandemic, the US explored taking on a leading role in medicine manufacturing. This was based on achieving a more reliable, responsive and safe medicines supply (Woodcock 2019). The range of aspects to consider for candidate locations is wide. Think of corruption (Xiao et al. 2018) and water stress (Settanni et al. 2019) to name a few. Probably enough to start questioning strategies based on back-of-the-envelope calculations.

Takeaway 1: How to know where specific APIs are made. Let’s consider a common API: paracetamol. Where is it made? Over a decade ago, we could find the answer in specialised industry and trade publications (Kirschner 2003). Now, market intelligence resources are sold dearly. Thanks to EU regulations, some information about manufacturers and importers is in the public domain. In Fig. 1 I tap into regulatory data to map out where the UK gets its paracetamol API from. There is no European supply since Rhodia closed its facility in 2009 due to poor profitability (Anonymous 2009). Paracetamol is now recommended for treating milder COVID-19 symptoms. As demand spiked in the UK, distributors feared that manufacturing issues might follow.
causing shortages (Andalo 2020). The footprint shown in Fig. 1 may help explain why.

2 Establishing a web of supply dependencies

We all have heard the statistics. China accounts for 14% of API and 8% of drug production in the US (FDA 2019: p 29). For the EU, press reports indicate that overseas dependence is as high as 80% (Laurent 2020) or 90% (Brunsden and Peel 2020) considering non-proprietary drugs. Loathing dependence on foreign production, both the EU and US are reconsidering their domestic API manufacturing capability (Geyman 2020). Few bother to add that it has been this way for longer than we think. Is the industry heading forwards or backwards?

Lesson 3: Over-dependency hides in plain sight. Scratching the surface, the claim of 90% dependence for the EU originated 12 years ago (EC 2020). The figure is an imprecise reading of an assessment developed for the Falsified Medicines Directive (CEC 2008). We also forget that until the 1980s the pharmaceutical industry was vertically integrated; since then, activities outside R&D and marketing are no longer core (Rees 2011). Evidence suggests that the manufacture of European APIs and intermediates has moved east since the end of the Cold War. This includes central and eastern Europe (Boswell 2007) and China (Boswell 2004). In the 2000s, overcapacity and low profitability kicked in due to slow demand and the proliferation of Chinese and Indian manufacturers (Pollak and Vouillamoz 2013). Single-country dependency did not happen overnight. It even made sense at some point.

Lesson 4: Successful reshoring decisions are primarily market-driven. Should we be wary of the current frenzy to bring manufacturing back? According to a survey, most businesses reshore to improve responsiveness, and get closer to customers (Srai and Ané 2016). Surprisingly, resilience is not as important a reason as one might expect. At least until now. Some reshoring ambitions might be easier to fulfil, as manufacturing technology has moved past large batch campaigns of blockbuster drugs. In particular, innovative continuous pharmaceutical processing enables shrinking factory scale, shorter lead times and better chemistry (Badman and Srai 2018). Manufacturing technology could help achieve resilience and patient-centric manufacturing. However, making a convincing business case for switching to, for example, continuous processing remains a challenge (McWilliams et al. 2018). We have addressed this topic more extensively in forthcoming work (Srai et al. 2020).

Takeaway 2: How to map current dependencies. There is lots of sensitivity about who supplies who in real-world manufacturing networks. Getting specialised information is onerous, and often requires a bespoke ‘bottom-up’ network mapping approach (Srai 2017). It may be quicker to proceed ‘top-down’ from freely available sector-level data.

Back to the cookies analogy, it is relatively easy to find out what goes into a £1 worth of total industry output – say ‘baked products’. Obviously, there is something wrong in approximating the whole industry with specific products and businesses. However, national statistics offices worldwide collect information about the former on a regular basis. One such dataset is a ‘World Input–Output Table’—WIOT (Timmer et al. 2015). In Fig. 2 I use WIOT data to show the foreign value-added share (FVAS) in the UK manufacturing and digital economy (for the details, see Settanni and Srai 2018).

According to Fig. 2, the UK foreign value added is contributed mainly by the EU (13.5% in 2013, with a slight decline in 2014). Indeed, 21% worth of competitive imports into the UK’s pharmaceutical sector originates in Germany and only 3.5% in China in 2013. Within the UK manufacturing economy, pharmaceutical manufacturing exhibits the lowest FVAS. This approach may be coarse, but gives a first approximation of the breadth of value dependencies in global manufacturing.

3 Matching demand and supply

Besides choosing a supply base wisely, picking up meaningful ‘demand signals’ can be extremely tricky. Unanticipated signals put manufacturing technologies to the test, challenging them to adapt and scale up in extreme operating conditions. In the case of APIs, these issues exposed an unreliable supply base. In the case of testing, they exposed the need to support production as it struggled to catch up with demand. Sector experts argue that over-reliance on China and India for the manufacture of APIs was old news to them. So why is it so difficult to make a convincing case for alternative manufacturing network configurations?

Lesson 5: The scale and adaptability demanded by extreme operational conditions may not be viable. Consider a nuclear power plant. A safe design will factor in the odds that an earthquake of a certain magnitude hits the area where the plant is built. But when things do not pan out as anticipated, we regret not having gone the extra mile with safety requirements (Silver 2013: Ch. 5).

Something similar is happening to manufacturing networks. Before COVID-19, sizing a manufacturing plant according to the highest anticipated level of demand meant freezing resources on idle capacity. After COVID-19, peak demand is dictating manufacturing expansion plans. For example, RNA extraction relies on a general-purpose bioseparation technology based on magnetic beads (Sinclair 1998). Whilst the technology could easily be repurposed, the

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scale of extraction kits required became evident as testing for COVID-19 progressed (Lim and Ehley 2020). A leading diagnostic equipment provider is expanding production of RNA extraction kits sevenfold (QIAGEN 2020). Regulators are also granting emergency use approval for alternative technologies that bypass RNA extraction. Yet, the diagnostic precision of these technologies is debated (Winter 2020). There is little concern about what is going to happen to the excess capacity when the storm has passed.

Lesson 6: Pre-emptive action might not pay off. Epidemiologists have warned that infectious diseases should be treated like national security threats— as with other threats, securing medical equipment, supplies, APIs and expertise deserves long-term investment and public will (Osterholm and Olshaker 2020).

This brings me back to an example in Silver (2013: pp.206–208). In 1976, the Ford administration in the US took resolute preventive action to secure $180 m worth of vaccines ahead of a pandemic that failed to materialise. Adding insult to injury, a rushed vaccine development program is believed to have caused neurological complications. Taking action on the basis of initial trend extrapolations may not pay off, and leaders can expect very little credit for taking preventive action (Bazerman and Watkins op. 2008). If successful, preventive action incurs tangible costs, and makes the costs avoided impossible to demonstrate.

Similar issues emerged whilst exploring drug repurposing in the absence of treatment for COVID-19. One of the candidates, chloroquine, was an assumedly cheap staple in the prevention of malaria (Principi and Esposito 2020). Anticipating a surge in demand, the only US manufacturer doubled its price (Kuchler 2020a). India, who manufactures most of the API needed for these formulations, decided to ban exports and prioritise internal use (Kuchler 2020b). Treatment for pre-existing patients was suddenly put at

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**Fig. 2** Decomposition of domestic and foreign value added for the UK manufacturing and digital economy based on analysis of data from World Input–Output Database. To save space, sector names are replaced by official NACE codes. Source: Settanni and Srai (2018)
Risk, without evidence that the drug is effective for its newly intended use.

Takeaway 3: How demand signals propagate across a supply network structure. Probably we all have heard of safety stocks. Put it simply, these are ‘buffers’ against demand variability during the time between placing an order and receiving it. One could think of it as the number of toilet paper rolls on top of a household’s weekly need—just to avoid running out of it between purchases. At the early stages of COVID-19 outbreak, toilet paper was in shortages in most stores. Based on the behaviour of some shoppers hoarding this product, their safety stock estimate must have gone through the roof.

On a serious note, thinking safety stocks is a really good way to link an uncertain demand with the intricacies of a manufacturing network. In Fig. 3 I’ve made up a fictitious pharmaceutical supply network with some information about each manufacturing location and the demand signal experienced closer to the market. Detail about how to answer the questions highlighted in red in Fig. 3 are beyond scope but the interested reader is referred to Graves and Willems (2000).

For now, it may be interesting to note the similarities between Fig. 3 and what most hospitals had to go through whilst facing the arrival of COVID-19 patients. Figure 4 shows a simple schematic I prepared to make sense of a possible strain on hospital resources due to different patient arrival scenarios.

The bell-shaped curve on the left-hand side of Fig. 4 is not the output of a fully-fledged epidemiological model. Yet, it is often used in practice. Many applications of advanced information technology and modelling aim to get that curve right (Naudé 2020). Figures 3 and 4 suggest that supply network analysis starts where those applications end.

4 Beyond ‘silver bullets’ and ‘bad apples’: improving situational awareness

When times are hard, it is tempting to look for ‘silver bullets’. Some promptly concluded that companies should rush through very specific technological transformations (e.g., Morgan 2020). It is also a deeply rooted belief that unacceptable outcomes must be due to morally wrong root causes (Hollnagel 2018). The same goes for disruptions related to COVID-19; hunts for ‘bad apples’ are often on (see e.g. Smith 2020; Mehta 2020).

Especially in times like this, it is worth recalling that we are not always in a position to claim than doing ‘a’ leads to ‘b’. In this spirit, I have tried to highlight that decisions about sourcing and manufacturing inherently expose supply chains to disruption. Targeted technology adoption, reshoring, and pre-emptive institutional action may have the charm of silver bullets, but I doubt these initiatives guarantee that we always get at our doorstep everything we need.

I find more intriguing that, despite the current abundance of information, reading clues in a complex environment remains difficult. We could look back at the events discussed above through the theoretical lens of situational awareness (Endsley 1995). For a pilot in the cockpit of a fighter jet, situational awareness is about perceiving relevant clues about a changing...
and challenging environment. Surely, plenty of clues are conveyed by the instrumentation. But which ones to pick? And what to make of it? Stitching together relevant clues, the pilot forms an integrated picture of the current situation. This also helps the pilot to make projections about future states.

Perhaps the dynamic reappraisal of location decisions in global manufacturing networks is not dissimilar from piloting a fighter jet. In both cases, the issue is how to convey relevant clues while avoiding undue cognitive effort. Tackling this issue can be tricky in the absence of what Cooley (2007) calls a ‘creative interaction between judgement and calculation’.

Back to the cookies joke with which we started, situational awareness might help us figure out when to start swapping recipes. But even then, we might have forgotten how to bake.

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