PROACTIVE AND REACTIVE INTERVENTIONS
TO MITIGATE MEDICINE SHORTAGES IN (AB)NORMAL TIMES

ABSTRACT

Purpose
The study aims to understand the relationship between proactive and reactive interventions to improve medicine availability in normal and abnormal times. We explore this relationship from supply chain risk management (SCRM) and supply chain resilience (SCRes) perspectives focusing on how they contribute to dealing with (potential) shortages.

Design/methodology/approach
We use an abductive approach and multiple data sources to map and compare interventions applied in the paracetamol supply chains of seven countries pre- and during COVID-19.

Findings
Interventions can be described along two dimensions: timing of planning and execution; we derive four intervention types based on these dimensions. We also find that interventions employed in normal times determine issues faced in abnormal times and the level of system changes required.

Research limitations/implications
Longitudinal primary and secondary data is used, but the complexity of the problem indicates a need for further, in-depth studies employing mixed method designs to ensure transferability of findings.

Practical implications
Decision-makers in the healthcare sector can use the findings when developing preparedness and response plans as well as risk management and resilience strategies for (ab)normal times.

Social implications
The insights developed can assist in striking a balance between proactive and reactive interventions to improve availability of generic medicines in (ab)normal times.

Original/value
The paper redefines boundaries between proactive and reactive interventions and how they can be leveraged for risk management and resilience in (ab)normal times. We also develop a model for studying and managing medicine supply chains in (from) normal and (to) abnormal times and vice versa.

Keywords: Medicine supply chain, medicine shortage, supply chain risk, resilience, interventions, COVID-19.

1. INTRODUCTION AND PURPOSE

"Paracetamol shortage will hopefully end in early 2019." (Zoio, 2018)

"There has been a significant increase in the demand for products such as paracetamol and ibuprofen over the last few weeks, which has caused some supply constraints."" (Andalo, March 13, 2020)

"….the European Union will seek to diversify its supply chains of medicines to reduce its reliance on other nations. "In practice this will mean stockpiling some crucial assets. It is not normal for example that Europe does not produce even one milligram of paracetamol," he [the EU Foreign Policy Chief Joseph Borrell] said." (Sheffi, 2020, p.211)

The quotes above illustrate two major problems in contemporary medicine supply chains: (i) shortage risk is high even in normal times where minor disturbances cause disruptions because of the complex nature of global supply chains and (ii) there are information gaps among key stakeholders potentially leading to less informed decisions (in fact, there is some paracetamol production in Europe). These issues demonstrate the urgent need to understand the drivers of medicine shortage problems and establish a solid evidence-based decision-making when developing strategies for normal and abnormal times (e.g., COVID-19).

COVID-19 has led to unprecedented disruptions in medicine supply chains worldwide, thereby exposing the multifaceted nature of their vulnerability at full scale (Ayati *et al*., 2020; Romano *et al*., 2021). The pandemic has demonstrated lack of preparedness for medicine supply disruptions in numerous countries (Sheffi, 2020). An extensive review of grey literature on pre-COVID preparedness in medicine supply chains in six European countries suggests that while many strategies were discussed, few had been implemented when the pandemic struck ([authors), 2021). This suggests proactiveness in the planning of interventions but a reactive approach with respect to their implementation. Furthermore, a review of the academic literature shows that surprisingly little research on medicine shortages had been published within operations and supply chain management (OSCM) before the pandemic (ibid.). *Hence, more OSCM research to understand risk mitigation and coping strategies to reduce medicine shortage is needed.*

The pandemic has resulted in an increased attention to supply chain risk management (SCRM) and supply chain resilience (SCRes) (e.g., Sodhi and Tang, 2021). Our literature review, presented in the next section, demonstrates that extant research does not provide a unified understanding of the two concepts; they are partly overlapping, partly distinguished, and it is not clear whether they handle different types of risks, or how they relate to the distinction between proactive and reactive interventions. This paper develops a framework that seeks to clarify these issues. In particular, we are interested in understanding the connection between SCRM and SCRes through the preparedness and response phases of disaster management. We pose the following research questions: *(i) What proactive and reactive interventions are applied in preparedness and response to pandemics in medicine supply chains; (ii) How do proactive and reactive interventions contribute to SCRM and SCRes strategies in normal and abnormal times, i.e., before and during the pandemic, respectively?*

Based on an abductive research approach (Dubois and Gadde, 2002; Kovacs and Spens 2005), we study the paracetamol supply chain in seven countries. To maintain rigor and enable a comparison across the different countries, we employed standardized tools for data collection and analysis while remaining open to exploring emerging themes. We selected paracetamol because it exemplifies an off-patent generic product distributed in large volumes globally which is susceptible to shortages. Our theoretical starting point for the study was linking mitigation strategies suggested in SCRM to interventions in medicine supply chains.

Our key contribution is to provide an alternative view on reactive and proactive interventions and, through this, the relationship between SCRM and SCRes in normal and abnormal times. We propose a model that transcends the debate on whether specific risk strategies are proactive, and others are reactive by showing that all strategies can be used proactively or reactively as appropriate. We suggest four intervention types: (1) Proactive/proactive - planned and executed proactively (most related to SCRM); (2) Proactive/reactive – planned proactively but executed reactively after a cue from the environment; (3) Reactive/proactive – planned reactively in direct response to an unforeseen change but executed before the change leads to shortages; and (4) Reactive/reactive – planned and executed reactively as fire-fighting measures (most related to SCRes).

We find that baseline interventions, i.e., those employed in normal times, directly impact the nature of issues faced in abnormal times and, hence, the level of system changes to be made through proactive/reactive and reactive/reactive interventions. Furthermore, our results demonstrate how investing in soft resources to create adaptability (e.g., in processes and relationships) during abnormal times can supplement or substitute investing in hard resources to create redundancy (e.g., strategic stock/own production) leading to greater gains in dealing with unforeseen crises while averting shortages. We also argue that both SCRM and SCRes can be improved through these interventions (or risk strategies as they are termed in SCRM) - it is simply a matter of timing. There are, however, questions about conditions under which such a strategy pays off for unforeseeable crises in terms of its cost-effectiveness. Our study provides a basis for further research on the cost-effectiveness of different types of interventions.

The rest of this paper is organized as follows. In section 2 we review the literature and, based on this, develop an initial research framework. The methods and preliminary results from our ongoing analysis are presented in sections 3 and 4 respectively. We conclude with a discussion of the findings, the proposed framework, and future research opportunities in section 5.

2. THEORETICAL BACKGROUND AND FRAMEWORK

Our theoretical starting point is informed by the early work on ‘robust supply chain strategies’ for handling risks in SCRM (Chopra and Sodhi, 2004; Tang, 2006) which were later expanded and refined based on findings from the humanitarian sector (Jahre, 2017). Table 2.1 shows the categories with examples of *interventions* (the term typically used in health research) to reduce medicine shortages.

Table 2.1 SCRM strategies (N.B. The letters in parentheses are used in the discussion below)

Strategy	Definition	Example interventions to reduce medicine shortages
Dynamic assortment planning (a)	Can be used to influence choice and demand, and to entice customers to purchase products that are widely available when certain products are facing supply disruptions.	Rationing
Economic supply incentives (b)	Encourage additional suppliers to stay or enter a certain market to avoid monopolistic situations, and to secure multiple sources should a disruption occur.	Back up supplier as secondary source in case primary has disruption
Flexible manufacturing process (c)	Allow for adjustments in quantity and quality produced in their network; for example, varying between plants and/or production lines.	Increase manufacturing capacity
Flexible supply base (d)	Multiple sourcing options available, thus allowing for alternatives should one source be disrupted. One way of doing this is to develop a supply alliance network with suppliers in various countries. Also called hedging.	Multiple suppliers for each medicine and/or Active Pharmaceutical Ingredient (API) (raw materials)
Flexible supply contracts (e)	Agreements with suppliers allowing the customer to adjust order quantities depending on need.	Framework agreement with flexibility on quantity/price
Flexible transportation (f)	Multi-modality, multiple carriers and/or multiple routes.	Prioritize transport of medicines, other routes/ modalities if borders close
Make-and-buy (g)	Combination of in-house and outsourcing, which allows more flexibility in case of a disruption. Includes vertical integration.	Establish own production at national, regional, European level
Postponement (h)	Utilises product or process design concepts such as standardisation, commonality, modular design, and operations reversal to delay the point of differentiation in products, services, movement, and other value-adding activities.	Allow foreign marking, other pack sizes; stockpiling API
Revenue management (i)	Dynamic pricing and/or promotion	Discounts, maximum price, step wise price
Silent product rollover (j)	'Leak' new products into a market without making formal announcements.	Substituting (change prescription) one medicine for another when shortage
Strategic stock (k)	Inventories at certain 'strategic' locations (warehouses, logistics hubs, distribution centres) that can be deployed quickly in case of a disaster. Often shared by multiple supply chain partners, e.g., vendor-managed inventory.	Emergency stock for essential medicines
Centralization (l)	Procurement, stocks, manufacturing, distribution	National procurement of medicines for COVID-19 treatment
Collaboration (m)	Risk sharing, supplier development, information sharing	Monitoring shortages and stocks
Speculation (n)	Opposite of postponement such as forward placement of inventory, forward buying, and early commitment to the form of a product.	National marking of medicines

There has been increasing research attention to SCRes to address supply chain disturbances (Ali *et al*., 2017; Wieland and Durach, 2021) but the connection to and distinction from SCRM is unclear. One perspective is that SCRM focuses on *maintaining* the supply chain despite disruptions, while SCRes is about quick *recovery* after disruptions have occurred (Tukamuhabwa *et al*., 2015; Wieland, 2021). Some researchers, on the other hand, seem to view the two concepts as essentially the same (e.g., El Baz and Ruel, 2021; Kamalahmadi *et al*., 2021; van Hoek, 2020). Bezhadi *et al*. (2020), for example, develop 'resilience metrics' for SCRM by focusing on 'time to recovery'. Similarly, Lücker and Fleischer (2017) study three classic SCRM strategies for 'building resilience'. There are also divergent views regarding the types of risks to be addressed by SCRM and SCRes. Some researchers suggest that SCRes is appropriate for addressing unforeseeable risks, whereas SCRM focuses on foreseeable risks (Ponomarov and Holcomb, 2009; Tukamuhabwa *et al*., 2015). Others adopt a SCRM lens on both types of risks, e.g., Ho et. al (2015) on normal and abnormal risks and Shekarian and Parast (2020) on operational and disruption risks. These inconsistencies make it difficult to distinguish whether strategies belong to either SCRM or SCRes, or to both upfront.

There are also conceptualization issues with respect to SCRM and SCRes constructs. Notably, strategy characterization in Table 2.1 as *redundancy* or *flexibility* is problematic. Kamalahmadi and Parast (2017) term pre-positioning inventory (k), backup suppliers and protected suppliers (b, e) as redundancy strategies (Table 2.1). Later they added multiple suppliers (d) and compare these with flexibility strategies [e.g., flexible transportation systems (f), and manufacturing volume flexibility (c)], pointing out that redundancy strategies are investments before a disruption, while flexibility [e.g., reserving capacity] does not require prior investment. Shekarian and Parast (2020) suggest that redundancy strategies include inventory (k), backup suppliers (b) and protected suppliers, whereas flexibility refers to the ability to adjust the supply chain configuration (e.g., g, h) in response to fundamental or long-term change.

It is also unclear which strategies are viewed as *proactive* (building preparedness ahead of a disruption) and which are *reactive* (responding to a disruption that has occurred). Bezhadi *et al*. (2021) suggest that *reactive* strategies include backup suppliers (b), capacity extensions (c), alternative markets (d), and flexible allocations (e) or flexible rerouting (f) strategies. Interestingly, all these strategies can be implemented ahead of a disruption. Rajagopal *et al*. (2017), on the other hand, conclude that *proactive* strategies include supply chain network design and risk propagation, sourcing/supplier selection and order allocation, reliable facility location/fortification and inventory management, and co-ordination, pricing and risk sharing contracts, which cover all strategies in Table 2.1. Hosseini *et al*. (2019) distinguish between absorptive capacity for *proactive* strategies (supplier segregation (b), multiple sourcing strategy (d), inventory positions (k)), and two groups of capacity for *reactive* strategies: restorative capacity (facility; manpower; technology restoration), and adaptive capacity (rerouting (f), backup supplier (b), communication(m)). Most of these are contradictory to Rajagopal *et al*.'s characterizations. Yang *et al*. (2021) conceptualizes *proactive* strategies as having more reliable suppliers, clear safety procedures, and preventive maintenance, while *reactive* strategies are operationalized as backup suppliers (b), extra capacity (c), alternative transport routes (f).

Four recent papers seek to clarify some of these issues. Wieland and Durach (2021) simultaneously connect and distinguish SCRM and SCRes by discussing two supply chain perspectives. They argue that traditional SCRM has its roots in engineering resilience and seeks optimality, *minimum time-to-recover and resistance to disturbance*. Social-ecological resilience, on the other hand, is more in line with SCRes and seeks *adaptability and supply chain structures that can absorb* maximum magnitude of disturbance. They suggest capturing both perspectives and define SCRes as "the capacity of a supply chain to persist, adapt, or transform in the face of change" (p.2). However, they do not address how this relates to

strategies. Roscoe *et al*. (2020) do this and use strategic contingency theory to define reactive strategies as "tactical and operational decisions that lead to tangible investments in variable assets aimed at reducing the severity of a risk event" (p.1503). *Proactive* strategies are defined as "strategic decisions that lead to tangible investments in fixed assets that change the supply network architecture and reduce or eliminate the probability of the risk event." (ibid.) They also suggest two additional categories – '*passive* strategies' which means doing nothing and then reacting chaotically and aimlessly after the event, while the '*wait-and-see* strategies' entail not making tangible resource commitments in advance but 'a deliberate commitment of intangible resources to acquire knowledge' (p.1504). In a similar vein, Sawyerr and Harrison (2020), based on theory from high-reliability organizations, distinguish between tangible (technical excess capacity in employees, facilities, transport, inventory, multiple suppliers, ICT, and power equipment) and *intangible* redundancy (supplier relationships, multi-skilled staff, continuity plans and multiple processes). Finally, Mackay *et al*., (2019) introduce ecology to separate between robustness and resilience, where the first concerns *proactive strategic investments* to maintain performance while the latter is about *strategic or operational ability to withstand* the effect of a disruption (see also Hosseini *et al*., (2019) on dividing decisions into operational, tactical, and strategic).

The above introduce key differentiators for mitigation strategies regardless of whether they are classified as redundancy/flexibility; proactive/reactive; robustness/resilience:

- the type of investments (tangible vs. intangible)
- the timing (before or during the event)
- the decision-level (strategic or operational)

Overall, there appear to be specific strategies and related interventions for mitigating or averting medicine shortages in normal and abnormal times. It is not, however, clear what interventions are proactive or reactive and how this affects the types of investments made, the timing (preparedness and/or response phases) and the level at which it is taken (strategic versus operational). We seek to better understand this relationship and how it further impacts SCRM and SCRes, what the relevant metrics are (e.g., flexibility versus redundancy) and their effects on medicine availability (or shortages) in normal and abnormal times.

3. RESEARCH METHOD AND DESIGN

Due to the lack of empirical studies on medicine shortages, we conducted an exploratory case study, which warrant exploring the phenomenon in a real-world context (Voss *et al*., 2002; Yin, 2018). We followed an abductive approach as it allows for an iterative process where empirical data directs attention to theory and vice versa (Dubois and Gadde, 2002; Kovacs and Spens, 2005). This was important as we, particularly in these times of the pandemic, did not know upfront what data was available in each country. We use an embedded case study design (Yin, 2018) to analyze the paracetamol supply chain in seven countries accounting for factors influencing outcomes with respect to shortages. The country's medicine supply chain is the main unit of analysis; seven countries constitute cases from which we can learn about interventions used in normal and abnormal times. Within this main unit of analysis, interventions to mitigate/resolve medicine shortages pre- and during COVID-19 are analyzed and linked to strategies, SCRM and SCRes.

We focus on paracetamol for palpability and tractability (Kim *et al*., 2015), e.g., to sufficiently map the supply chain and achieve comparability among countries. Paracetamol products are highly used worldwide, both in high (Wastesson *et al*. 2018) and low/middle- ((Kabba *et al* 2020; Mayora *et al*. 2018; Sillo *et al*. 2018) income countries. Paracetamol is an active ingredient used for producing painkillers which are used globally for mild to moderate pain such as headaches, toothaches, muscle- and joint pain. It is an off-patent generic medicine, thus representing the class of medicines which has seen the largest increase in shortages in recent years (Scholz 2020; DiPiro *et al*. 2021). In general, though, high volume products like paracetamol formulations are more robust against shortages than low volume products, e.g., certain antibiotics. It comes in different strengths, pack sizes and forms (tablets, oral, suppositories, infusion, oral suspension), is used in primary and specialist (secondary) healthcare both for adults and children. It is both prescribed and non-prescribed and, in most countries, also sold outside of pharmacies such as in grocery stores. Despite its widespread use and importance, there has been relatively limited research on paracetamol supply chains (c.f., Kabba *et al*., 2020; Kefale and Shebo, 2019; Mayora *et al*., 2018; Schiavetti et. al. 2018; Sillo *et al*., 2018; Tujo and Gurmu, 2020). We could not find research specifically on paracetamol shortages in the prior literature.

Figure 3.1 illustrates the research process in line with Kovacs and Spens (2005). We searched the Web of Science (WoS) database for studies on paracetamol, medicine shortage, and recent SCRes and SCRM studies. We used the results from that literature review to shape the data collection tools and to analyze our data. We sought to address the data availability challenges hampering SCM research on adverse events (Kim *et al*., 2015; Melnyk *et al*., 2014) by analyzing reliable secondary sources and then building on those findings for the interviews. We used a standardized set of data collection and analysis tools, across the seven cases, for mapping causes of shortage and either suggested or implemented interventions, a common framework for analysis and nomenclature ([authors], 2021). The data was recorded in a pre-structured excel workbook which was periodically adjusted as new themes emerged from the secondary and interview data sources. A standardized template for case description (arrived at through several iterations) and a study log was kept by all data collectors.

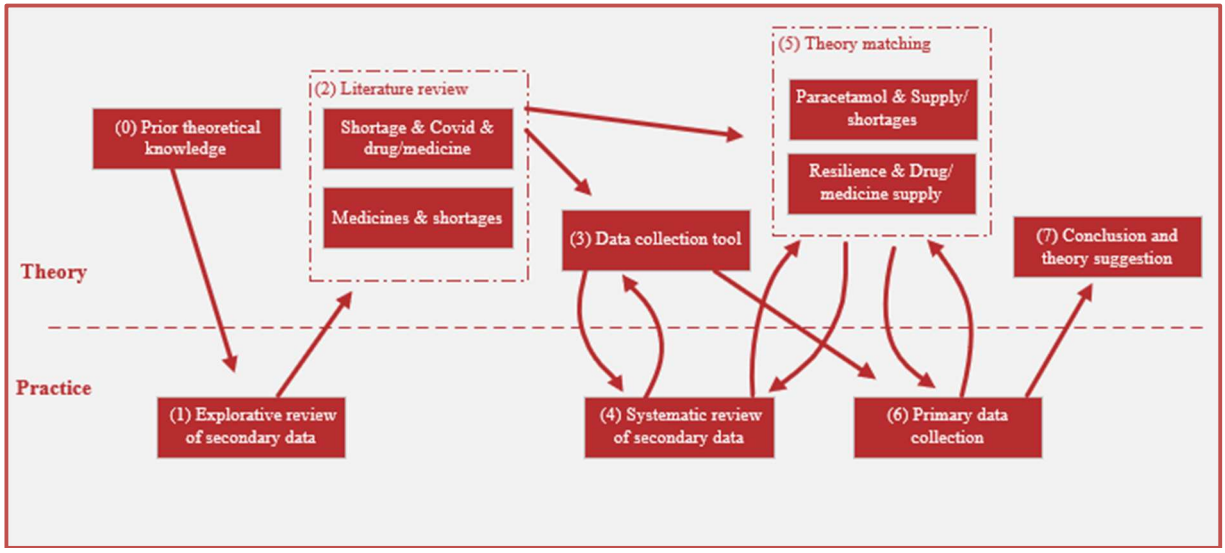

Figure 3.1: The abductive research design

In addition to secondary data collection, we conducted 63 semi-structured interviews between October 2020 and May 2021. We developed a common interview guide (see Appendix A), although this was used flexibly to take into consideration country specificities and associated secondary data sources. The guide was tested through pilot interviews and revised accordingly. Data availability was a challenge in some countries, particularly regarding statistics on product demand and shortages. When data was lacking or publicly unavailable, we used the interview data to qualitatively assess shortages before and during the pandemic. We conducted both within- and cross-case analyses. We first analyzed the data per case (country) and developed high-level supply chain maps for generic medicines, and specifically for paracetamol. We subsequently combined the populated excel workbooks per country regarding the context pre-COVID, and potential shortage problems and interventions during COVID to develop cross-case analysis tables. These tables helped us to discern similarities and differences between countries on key dimensions, e.g., distribution models and strategies used to mitigate shortages. In this way, we were able to assess qualitatively if and how shortages were averted.

4. FINDINGS

In this section, we first illustrate and discuss the generic paracetamol supply chain structure, highlighting differences and similarities between the seven countries. Second, we present preliminary results on key dimensions of the country-specific context pre-COVID; interventions suggested or implemented pre-COVID and during the pandemic as well as what the countries plan to do post-COVID.

Paracetamol comes in different strengths, pack sizes and forms (tablets, oral, suppositories, infusion, oral suspension), and is used in primary and specialist (secondary) healthcare both for adults and children. The most common paracetamol product is the 500 mg tablet in 20-pack size. Figure 4.1 shows an abstracted paracetamol supply chain structure based on our analysis of key supply chains for this medicine across the seven countries in focus.

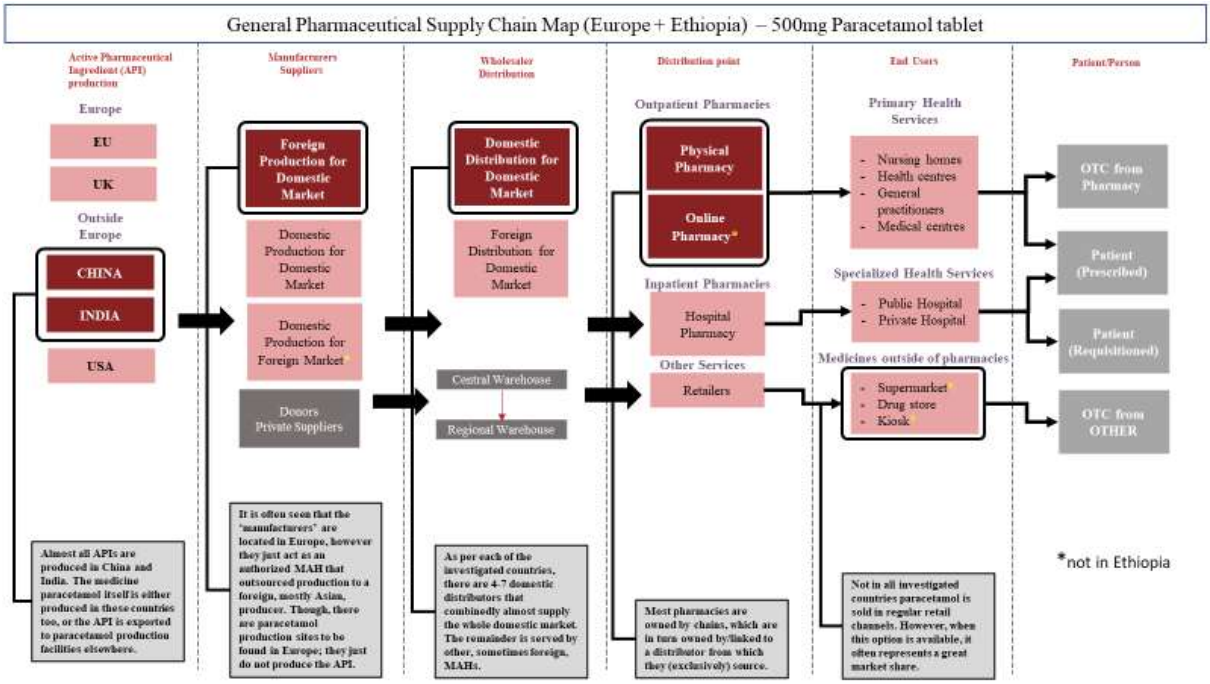

Figure 4.1 General supply chain map for 500 mg. paracetamol tablets

The individual country supply chain maps share many similarities in terms of key supply chain actors such as Market Authorization Holders (MAH - those who are licensed to sell), Active Pharmaceutical Ingredients (API) suppliers, as well as distributors and wholesales further downstream. In the European market, most countries import the paracetamol API from China and/or India. Furthermore, paracetamol manufacturers tend to be based in Europe, but they offshore or outsource manufacturing entirely to foreign, low-cost countries like India or Vietnam. European paracetamol markets are mainly dominated by a handful of distributors, who supply medicines to hospitals, pharmacies, health centers and other pharmaceutical organizations. The different supply chain maps do, however, not look completely similar. There are some notable exceptions: the UK is the only country with paracetamol API production; Belgium, France and the UK have European production facilities; France and Belgium were the only countries that did not sell paracetamol through other retail channels, such as in supermarkets, gas stations or kiosks, although France implemented it in January 2020. Ethiopia has local production capacity, but also gets paracetamol from donors or private suppliers in case of supply issues.

Table 4.1 displays an overview of contextual differences and similarities between the seven countries. Patients receive their paracetamol based on prescriptions or buy it as an over-the-counter medicine (OTC). Two main distribution models are direct-to-pharmacy (DTP) and multi-channel systems (Leth *et al.* 2019). In DTP, the manufacturing company assumes the MAH role and contracts a 3PL provider that distributes their product to all potential distribution points. In multi-channel systems, a wholesaler purchases the products from the manufacturing company and assumes the MAH role. This results in multiple wholesalers providing the same product.

Table 4.1 Key dimensions of the paracetamol supply chain – the context table pre-COVID

Country	United Kingdom	France	Belgium	Netherlands	Norway	Sweden	Ethiopia
Distribution points							
Health care system							
Pharmacy							
Retailers							
Distribution model							
Multi-channel							n/a
Direct to pharmacy							
Stock levels & shortage monitoring							
Regulated stock-/ safety stock-levels	Framework agreements on supply, penalty regulated	Framework agreements on supply, penalty regulated	No	Framework agreements on safety stock	1-6 months depending on product	Framework agreements on supply, penalty regulated	TBC
National Shortage monitoring							
Publicly available information on shortages	Serious shortage protocols are publicly available	Limited shortage protocols	List of current shortages	List of current shortages	List of current & historic shortage registration	List of current & historic shortage registrations	Information in health commodity information system & platform
Market & country information							
Market size, generic medicines	78%	80.9%	67% (TBC)	77.9%	51.10%	62%	91%
Population/ Population density	66 M/ 279 p/km^2	67 M/ 104 p/km^2	11.5 M/ 384 p/km^2	17.3 M/ 517 p/km^2	5.4 M/ 15 p/km^2	10 M/ 25 p/km^2	110 M/ 115 p/km^2
Number of outpatient pharmacies	11539	20966	4797	2000	1001	1433	6292

Product development, manufacturing and distribution is often carried out by global, private-sector actors. Further downstream, products are financed through public funds in different reimbursement-based and benefits programs. The domestic supply chain is mostly regulated by public authorities, but this differs between countries. The medicine market is regulated in many ways e.g., the MAH's license is limited to one product with a specific packaging, so once the product is packaged, it is dedicated to one market.

The procurement process for medicine is complicated and difficult to describe in general terms due to the many different distribution points and systems in each country. Sweden and the UK have regional procurement organizations that set up framework agreements and France has a central agency with the same responsibility. A maximum price is mostly set by national authorities in various reimbursement and benefits programs, but they do not include all paracetamol products. OTC products are, for example, often procured by the individual company. In the UK, a maximum price is only set for the contracted supplier in secondary care settings. The Netherlands has a private version of the benefits program where the insurance company contracts a preferred supplier for their customers. Stock levels and safety stock in the medicine supply chain are also regulated in some cases. Norway, for example, has a national directive for specific products with stocks covering average demand for 30, 60 or 90 days. Other countries, for example the Netherlands have no national regulations, but suppliers maintain 4-6 months of safety stock.

Pre-COVID, the sampled countries had shortage monitoring and some intervention strategies in place. However, they use different shortage definitions, making it challenging to compare and communicate issues with each other. All countries apart from Belgium had conducted a holistic risk analysis of medicine and vaccine shortages before the pandemic struck. Most countries had subsequently initiated a project for developing a holistic strategy but only two (Ethiopia and the UK) had fully implemented it by December 2019. Ethiopia and UK also had general preparedness strategies with the UK focusing on potential implications of a no-deal Brexit and Ethiopia focusing on secure supply more generally through, for example, increasing local production of essential medicines over time. Interestingly, we find that no country had analyzed the cost-effectiveness of the (potential or implemented) interventions. Norway, Sweden, and the Netherlands explicitly had discussed the need for such analysis.

Although there were serious concerns about paracetamol availability as a result from COVID-19, only two countries reported worse than usual shortages: Belgium and Ethiopia. Downstream hoarding, export bans and API shortages impacted most countries. Although most countries had manufacturing capacity constraints, Ethiopia uniquely reported repurposing of manufacturing as having a negative impact on supply: some paracetamol manufacturers switched to sanitizer manufacturing. Overall, some challenges were similar, others were unique, and still, most countries were able to avert shortages.

Table 4.2 summarizes the interventions taken before, during, and planned for after the COVID-19 pandemic ends. We could distinguish intervention strategies that were conceived either pre-Covid (e.g., as part of the aforementioned risk analyses different countries conducted pre-Covid) or as a result of Covid-19 in response the challenges posed by Covid-19. In Table 4.2, these intervention strategies are presented under "Conception" and marked as either Pr (i.e., pre-Covid) or D (i.e., during or as a result of Covid-19). We could further distinguish three moments of execution of these strategies and this is reflected under "Execution" in Table 4.2: before Covid-19 (Pr), during or as a result of Covid-19 (D) and planned or under discussion for implementation post-Covid (Po). Thus, there was a spectrum of conception/implementation strategies ranging from purely proactive (conceived and implemented pre-Covid) to purely reactive (conceived and implemented during Covid-19).

Table 4.2 Shortages, interventions during 2020, and planned/suggested interventions from 2021

APPROACH	EXAMPLES OF MEASURES	INTERVENTIONS					COUNTRIES						
		Conception		Execution									
		Pr	D	Pr	D	PO	BE	ET	FR	NL	NO	SE	UK
Dynamic assortment planning	Rationing at consumer level	✓		✓			●		●	●	●		●
		✓			✓							●	
	Conscientize downstream customers about hoarding impact		✓		✓		●			●	●	●	●
Economic supply incentives (+) and disincentives (-)	Ban parallel exports (+/-)	✓		✓							●		
	Tendering process (+/-)	✓		✓								●	
	Freedom of pricing (+)	✓		✓									●
	Volume commitment contracts (-)	✓		✓									●
	Annual licence fee (-)	✓		✓									●
	Reward systems that minimise supplier penalties (+)		✓			✓							●
Flexible manufacturing processes	Improve API availability		✓			✓							●
	Scalability (in design)	✓		✓								●	●
			✓		✓				●				●
			✓			✓							●
	Increase of repurposing (in design)	✓		✓			●						
			✓		✓		●						●
Flexible supply base	Increase local production		✓			✓			●				
	Measure flexibility at API level		✓			✓							●
	Dual or multiple sourcing	✓		✓			●			●	●	●	●
	Staggered tendering (e.g., regional)	✓		✓									●
	Regulatory flexibility (buying out of licence)	✓		✓									●
Flexible supply contracts	Expand criteria to include resilience metrics		✓			✓							●
Flexible transportation	Import exemptions	✓		✓			●						
	Prioritise transport (modes) (e.g., subsidize/pay more)		✓		✓		●		●		●	●	●
Make-and-buy	Domestic manufacturing and imports (e.g., by wholesalers)	✓		✓									●
			✓		✓						●		
			✓			✓	●	●	●	●	●		●
	Relaxation of buying regulations		✓		✓								●
Postponement	API strategic stocks		✓			✓							●
	Increased expiry date, preparation for repackaging		✓			✓						●	
	Allow foreign marking										●		
Revenue management	Increase maximum price	✓		✓							●		
	Temporary limit-order-prices increase		✓			✓						●	

Continuation of Table 4.2 Shortages, interventions during 2020, and planned/suggested interventions from 2021

APPROACH	EXAMPLES OF MEASURES	INTERVENTIONS					COUNTRIES						
		Conception		Execution									
		Pr	D	Pr	D	PO	BE	ET	FR	NL	NO	SE	UK
Silent product rollover	Substitution	✓		✓			BE				NO	SE	UK
			✓		✓				FR				
Strategic stock	Emergency / strategic stock	✓		✓			BE		FR		NO		UK
			✓		✓		BE			NL	NO		UK
			✓			✓						SE	
	Increased turnover safety stock		✓			✓						SE	
Centralization	Centralized procurement	✓		✓							NO	SE	UK
			✓		✓							SE	
	Centralized strategic / Buffer stock	✓		✓									UK
Collaboration	Information sharing / communication	✓		✓			BE						
			✓		✓							SE	UK
			✓			✓	BE		FR				
	Joint procurement		✓			✓				NL		SE	
	Joint planning / decision-making	✓		✓									UK
			✓		✓							SE	UK
	Sharing (scarce) supplies		✓		✓					NL			UK
	Risk-sharing		✓		✓							SE	
Speculation	Decoupling API bulk contracts		✓		✓		BE						
	Allow foreign marking / labelling		✓		✓				FR			SE	
	Material & product purchases	✓		✓									UK
			✓		✓							SE	
Monitoring	Monitoring usage and availability	✓		✓			BE		FR		NO	SE	
			✓		✓							SE	
Adaptation	Streamlined processes (e.g., granting licenses, monitoring)		✓		✓							SE	UK
	Information and communication hierarchies		✓		✓								UK
Price regulation	Price-setting for major manufacturers		✓			✓			FR				

Most strategies used are in line with prior research, but there are widespread differences with regard to when and how the different countries implement them. For example, all countries rationed supply as a *dynamic assortment planning* tool in response to downstream hoarding, but this was implemented at different levels. Some countries (e.g., UK, Sweden, Norway) also already limited supply downstream for safety reasons and merely tightened these restrictions. Under *collaboration*, the Netherlands is advocating a future purchasing pact to curb China's increasing power in the supply chains of generic medicines, while Norway aims for a joint Nordic tendering process hoping to increase supply security. During the crisis, most countries allowed re-packing and re-labelling, which could be viewed as an example of *postponement*.

There are also discernible differences in the types of resource investments and decision-levels for the different intervention strategies. Most pre-Covid intervention strategies, implemented before or during Covid-19, entail investment in, or deployment of tangible resources. In contrast, strategies in response to Covid-19, implemented before disruptions were encountered or after, were generally taken at national level and use a mix of resources (e.g., collaboration and rapid deployment of resources to mount a timely response are of equal importance). There are some exceptions to this. For example, most supply incentives are relationship based and entail less upfront investment in tangible resources. There are also differences in inertia (which can be a proxy for agility) across countries. While Ethiopia and UK stand out in terms of implemented intervention strategies pre-Covid, it is also apparent that the UK was much more adaptive in terms of responding to Covid-19 and beyond. Ethiopia had plans to ramp up local production for essential medicines pre-Covid but actually produced less paracetamol during Covid-19 and still has plans to address this in the future. This suggests major resource differentials affecting the link between foresight and timely action.

5. CONCLUSIONS, IMPLICATIONS AND FURTHER RESEARCH

This paper has sought to increase our understanding of the relationship between SCRM and SCRes by linking preparedness and response strategies with proactive and reactive interventions to improve medicine availability in normal and abnormal times. Based on the literature review, we explored this relationship focusing on how interventions contribute to dealing with (potential) medicine shortages in different settings. Based on strategies suggested in SCRM, we developed standardized tools for data collection and analysis of paracetamol supply chains in seven countries and subsequently expanded the analysis to incorporate SCRes aspects. Our main finding is that, overall, the observed interventions combined strategies which were specified proactively (as part of general risk management) or reactively (in response to the COVID-19 pandemic). Furthermore, these interventions, i.e., strategies were executed either proactively or reactively.

From Table 4.2, it appears that interventions employed in normal times, are more consistent with SCRM. They also directly impact the nature of issues faced in abnormal times and, hence, the level of system changes required through proactive/reactive and reactive/reactive interventions. Proactive/proactive measures lead to high robustness in the system at baseline, which can result in less pressure to adapt quickly (agility) but might require flexibility, nonetheless. We also find that future interventions, i.e., post-COVID, are largely in the conception phase (proactive strategy formulation), yet to be implemented. Time will tell if they will be implemented in a proactive or a reactive fashion, but it is worth discussing the potential implications of either approach. We discuss this and other issues at length in this section.

Our study shows that in SCRM terms, the countries were not well prepared for the disruptive effects of the pandemic on medicine supply. This is in line with the reports from reputable news agencies and government publications during last year after the pandemic struck. Consistent

with the supply chain resilience literature, most countries had to adapt in order to cope with and overcome the threat of paracetamol shortages. Agility was even more important for those countries without any redundancy or robustness to deal with a sudden disruption in supply. An intriguing finding is that Ethiopia, as the only low-income country studied, was seemingly more prepared having proactive/proactive measures in place. It is only comparable to the UK in this regard. However, Ethiopia, along with Belgium, were the only countries that experienced serious paracetamol shortages. We speculate on two key implications of this finding.

First, *general preparedness leads to better outcomes than specific preparedness*. Several countries had prepared specifically for epidemics (including, interestingly, the UK and France) but, because they prepared for the wrong outbreak (wrong disease and also turning out to be a global pandemic), their SCRM strategies were of little benefit in responding to COVID-19. Some of this was caused by system exhaustion as, at some point, stocks stopped being rotated and either expired (UK) or were taken away and not replaced (France). General preparedness strategies were in place in the UK (because of Brexit) and Ethiopia (likely because of frequent disruptions due to natural disasters and insurgency), and this was a positive aspect linked with both SCRM (mitigating known risks) and SCRes considerations (dealing with the unforeseeable).

The second key implication is that *resource-poor systems with weak infrastructure will suffer greater setbacks than those with good infrastructure*. Agility can be hindered by a lack of funding as resources often have to be deployed quickly to enable this, while flexibility cannot be easily achieved if there were infrastructural issues that would take multiple years to resolve even if funding became available. In Ethiopia, transport challenges made it difficult to deliver paracetamol to where it was needed, the country has weak health supply chains also in normal times, and there is generally greater dependency on donor agencies to implement interventions.

Another interesting observation from the study is that while most countries had not implemented the strategies they explored through evaluations conducted pre-COVID (most even lacked physical preparedness, e.g., in terms of emergency stocks), they were able to adapt when the pandemic struck based on the results from the evaluations. Decision-makers in most countries we studied had considered a variety of strategies (proactive formulation) but had problems with getting funding without the appropriate evidence-base. With COVID-19, the problems they foresaw became more visible and this accelerated the disbursement of funds leading to, for example, emergency stockpiling. Stated differently, the proactively formulated strategies were implemented reactively, and this was still sufficient to enable most countries to avert shortages despite the upstream disruptions that they encountered. Although this funding reluctance appears to be a major issue, another way of looking at this is that this planned, "wait and see" strategy, may be sensible if the occurrence of future events cannot be predicted with certainty. Implementing costly strategies only when they are needed and doing so swiftly appears to have been a good alternative to the cost-robustness trade-off.

Our results also demonstrate how investing in soft resources to create adaptability (e.g., in processes and relationships) when abnormal times occur can supplement or substitute investing in hard resources to create redundancy in normal times (e.g., strategic stock/own production) leading to greater gains in dealing with unforeseen crises while averting shortages. Also noteworthy is that better preparedness appears to enable improved future planning. As a crisis play out, particularly a protracted one as COVID-19, there is ample opportunity to learn about effectiveness of strategies and their implications. In our study, countries that had formulated more proactive measures (which can subsequently be executed either proactively or reactively) also seemed to be better-positioned to think ahead on managing risks for similar future events, i.e., be more generally prepared, as opposed to preparing for another COVID-like pandemic.

Our research questions were formulated as follows:

(i) *What proactive and reactive interventions are applied in preparedness and response to pandemics in medicine supply chains?*

(ii) *How do proactive and reactive interventions contribute to SCRM and SCRes strategies in normal and abnormal times, i.e., before and during the pandemic, respectively?*

Above we have discussed our findings in relation to the research questions. Our key conclusion is that both SCRM and SCRes can be improved through these strategies – it is simply a matter of timing. Our key theoretical contribution is depicted in figure 5.1: A model that transcends the debate on whether specific risk strategies are proactive, and others are reactive, by showing that all strategies can be used proactively or reactively as appropriate. We suggest four intervention types:

- proactive/proactive – specified and executed proactively (most related to SCRM)
- proactive/reactive – specified proactively but implemented reactively
- reactive/proactive – specified reactively (in this study, specifically in response to Covid-19) but executed proactively to mitigate risks
- reactive/reactive – specified and executed reactively (most related to SCRes)

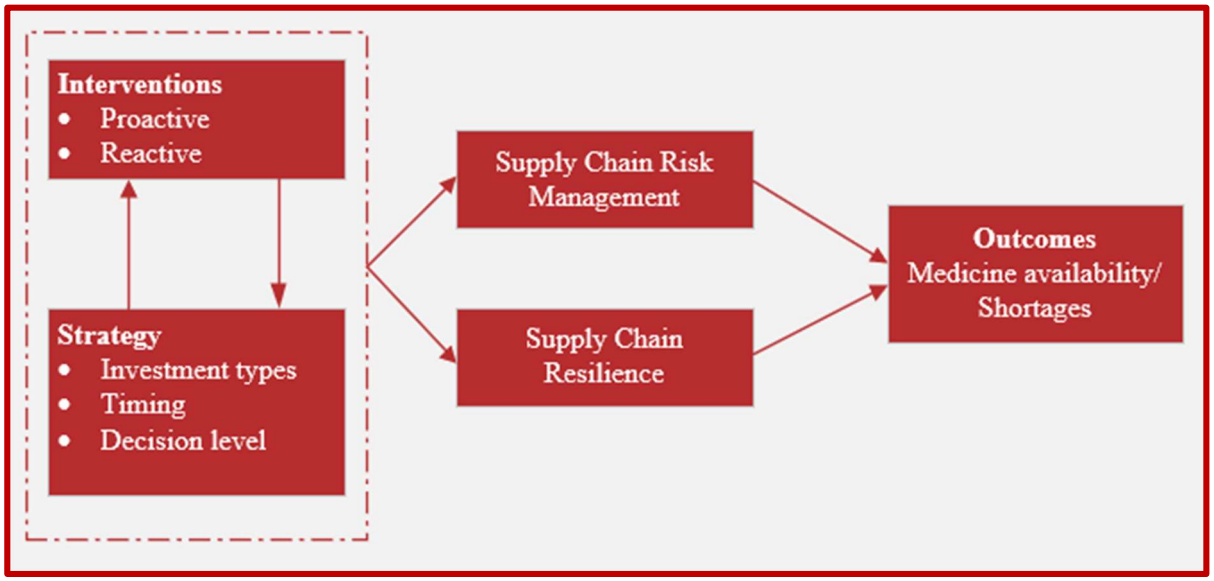

Figure 5.1 Suggested research model: key relationships and link to SCRM and SCRes

In terms of policy and social implications, we find that most of the countries we have studied seek to develop strategic stocks and investigate possibilities of bringing production back either at national or regional level (e.g., Nordic or European). In other words, these countries seem to focus on redundancy strategies to improve robustness. Contrary to this, our findings suggest that for future interventions, sustainable and cost-effective strategies for abnormal times could entail less focus on redundancy strategies. To this end, emphasizing more lessons learned from

the COVID-19 experience about rapid adaptation to, and recovery from, unforeseeable situations is essential for three primary reasons. First, building redundancy to cope with the next pandemic might be a costly and risky strategy as the next crisis might be very different from COVID-19. Second, because redundancy strategies are costly and pandemics are (historically) rare occasions, they are commonly abandoned when pandemics are distant memories. Third, if all countries opt for redundancy strategies, mainly building emergency stocks, this might further trigger shortages in normal times and exacerbate the situation for low-income countries that are already greatly disadvantaged when it comes to equitable access to essential medicines.

Suggestions for further research are plentiful from our initial findings and we will mention a few here. Firstly, we will continue data collection to corroborate results with more interviews and discussions with key stakeholders in the countries. More in-depth studies, also including post-COVID situations, will contribute to an improved understanding of how interventions are linked, overlapping, and counteracting. Secondly, we encourage future research to replicate our study on other medicine types with different characteristics, and other countries where the context might differ from the ones we have included. Finally, future studies should include comparative analysis of cost-effectiveness of the studied interventions to support decision making with respect to policy formulation and /or enactment.

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APPENDIX A: THE INTERVIEW GUIDE USED

1. Can you describe what your organization does in normal times and in case of crises when it comes to medicine supply (e.g., COVID-19)?
    a. In the supply chain ranging from manufacturers to patients/consumers, where is your organization and which stakeholders do you interact the most with? [Show supply chain map that we drew]
        i. Do you think this pharmaceutical supply chain draft correctly represents the current chain?
        ii. Where do you think bottlenecks occurred in the supply chain (if they did) during COVID19? Was this a change compared to pre-COVID?
        iii. How is information shared among stakeholders? How efficient / quick is it? Do you think there is a better way? If so, why in your opinion isn't it changing?
    b. What kind of supply chain decisions does your organization make (e.g., placing orders, managing stock levels, transporting medicines, setting prices)?
    c. Does your organization have a specific role/assignment in connection to medicines shortages?
2. Can you describe your role in your organization?
    a. Which part of the supply chain (we talked about in the previous question) are you focused on (e.g., placing orders, managing stock levels, transporting medicines, setting prices)?
    b. What kind of decisions do you make with respect to this part of the supply chain?
3. What actors do you consider to be central for the national medicines supply?
    a. Could you comment on this map of the paracetamol supply chain(s) – does it reasonably reflect the supply chain(s) in which you take part?
    b. Do you have any information on stock levels, lead times (in rough numbers) and transportation modes used in the SC?
4. Was shortage (potential or actual) a problem before covid-19? Which products in particular? If yes, could you elaborate on probable causes and what has been done to solve the problem? What did you/your organization do in this regard? What was the results/expected results from these actions?
5. Has availability of paracetamol changed (more potential or actual shortage), during covid-19? Did you expect such changes? Why/why not?
6. In case of more (potential or actual) shortage, could you provide some notable examples, and elaborate on (probable) causes and what has been done/will be done to solve the problem?
    a. The causes: supply/demand/distribution/market
    b. The interventions: what did you do and how quickly did you respond? Had these interventions already been discussed in connection with improving preparedness in general, i.e., pre-COVID?
    c. Has the problem changed during the pandemic (1st, 2nd, 3rd Wave)? Have the interventions changed?
    d. What do you/your organization do in this regard?
    e. What would you have done differently now that you know what happened?
    f. What other actors have been central in this response?
    g. What interventions affected your organization the most? Why? Do you think other organizations were affected the same way?

7. [What was the most urgent change / biggest risk before the COVID (not in terms of shortage necessarily)]
8. What do you consider are the challenges in managing the paracetamol supply chain with respect to securing availability at pharmacy/hospital/other outlets (i) in general and (ii) during the pandemic (waves)?
9. What would make it easier to prevent shortages? Did you become aware of any of these measures as a result of the pandemic? If so, which ones?
10. We are particularly interested in ongoing or potential cooperation between countries on supply chain relevant activities:
    a. Joint procurement
    b. Joint strategic stocks
    c. Joint agreements on investment and establishment of own production
    d. Joint transport or other agreements
    e. Other initiatives or ideas for sharing (tangible and non-tangible) resources across countries/regions to avoid shortages?
11. What about competition? Did you experience export bans, increasing prices, discussions with other countries?
12. Is there anyone else we should speak with?
13. Any other follow-up questions that the country lead might wish to ask based on the analysis of the grey literature and the quantitative analysis of product usage /shortage data e.g., questions regarding funding, information flows, or specific interventions.