Received 26 April 2024
Revised 29 August 2024
24 January 2025
24 March 2025
22 May 2025
Accepted 22 May 2025

An investigation of Dutch pharmaceutical supply chains: insights from the theory of swift and even flow

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Abstract

Purpose – This study aims to identify the main inhibitors limiting product flow across different stages of the pharmaceutical supply chain (PSC) and examine how they influence drug availability.

Design/methodology/approach – Semi-structured interviews were held with actors at different stages in the PSC. The theory of swift and even flow (TSEF) is used to ground the insights obtained from multiple actors across the PSC and formulate propositions for further research.

Findings – It is observed that most risk drivers hindering the swift and even flow of products – and thus threatening drug availability – are related to variability. Variability originates mainly from the regulatory environment in the form of non-value-added tasks and bottlenecks and, to a lesser degree, from the competitive environment. Our findings suggest that regulatory measures taken to reduce the cost of drugs, such as price law changes and tender frequencies, might create unintended consequences affecting drug availability. This highlights the impact that public policymakers have on drug availability.

Originality/value – This study, in contrast to previous research, investigates the movement of drugs through multiple stages of the PSC and identifies the operating environments that hinder product availability using TSEF. Benefiting from the constructs of TSEF, this study extracts and structures the findings from expert interviews and formulates research propositions to create a better understanding of the factors influencing drug availability.

Keywords Pharmaceutical supply chain, Supply chain risk, Drug shortages, Theory of swift and even flow

Paper type Research paper

1. Introduction

Drug availability is widely recognized to be of vital importance to societies. The COVID-19 pandemic and associated product shortages in healthcare have brought new attention to the

Funding: This project is partially funded by TKI Dinalog (Dutch Institute for Advanced Logistics) under grant number 2020-2-235TKI.

The International Journal of Logistics Management
Vol. 36 No. 7, 2025
pp. 262-283
Emerald Publishing Limited
e-ISSN: 1758-6550
p-ISSN: 0957-4093
DOI 10.1108/IJLM-04-2024-0266

importance of drug availability (Shuman *et al.*, 2020). Not only did the pandemic trigger additional drug shortages and exacerbate scarcities in many countries (Smith, 2020; EAHP, 2020) but it also highlighted the need to examine vulnerabilities in pharmaceutical supply chains (PSCs) (Vogler, 2024).

PSC disruptions and drug shortages have inspired several international research initiatives, such as COST (2020) and EAHP (2020). Despite the widespread notion that the potential consequences of supply chain (SC) vulnerability are not limited to the weakest link (Slone *et al.*, 2007), most of the empirical research on the PSC has focused exclusively on only a single part of the supply chain (Abdulsalam *et al.*, 2015) and/or on specific pharmaceutical products (Su *et al.*, 2018). Prescriptive research on the PSC typically formulates operational problems and optimizes decision-making in such networks (see, e.g., Abdolazimi *et al.*, 2021) or examines the performance (productivity) of actors for specific products or processes in the PSC (see, e.g., Ahlqvist *et al.*, 2023). In summary, the research identifying PSC risks and causes of shortages has not explicitly considered their relationship with product flow across the entire PSC, even though managing product flow is of key importance to the operational performance of a supply chain (Schmenner and Swink, 1998).

The objective of the current paper is to address the issues above, by formulating the following research question: What are the main inhibitors limiting product flow across different stages of the PSC and how do they influence product availability? We frame our analysis through the lens the theory of swift and even flow (TSEF) because it explains productivity gains through the reduction of process variability, non-value-added tasks, and bottlenecks that hinder a stable and speedy product flow (Schmenner and Swink, 1998). TSEF has been used in previous studies to analyze firm or supply chain *productivity* (Eltantawy *et al.*, 2015; Fredendall *et al.*, 2009; Murat Kristal *et al.*, 2010). We, however, focus on improving product *availability*, which is the key concern in the PSC due to the criticality of its products. Studying the impact of even flows across different actors in the value chain is especially relevant in supply chains characterized by a high degree of complexity, such as those in PSCs. To this end, we interview actors at different supply chain echelons in global pharmaceutical networks.

We focus on the PSCs that supply the Dutch market, i.e., the Dutch PSC. Selecting the PSC of a single country as the unit of analysis allows us to control for the impact of national regulatory aspects within a global network. The pharmaceutical sector in the Netherlands is characterized by a dense supply network of private actors competing in a market governed by public actors. The Dutch PSC is therefore a good illustration of how the interactions between a highly competitive network of suppliers and public governance mechanisms can influence the swift and even flow of products that affects drug availability. In addition, the Netherlands accounted for 15% of the annual 22,487 shortage notifications across the European Union (EU) (European Commission, 2021), making it a suitable case study to investigate drug shortages.

This paper makes two contributions. First, we identify key factors that affect product availability across multiple stages (rather than a single stage) of the PSC using TSEF as a theoretical lens. Second, we conjecture how the interaction between these factors influences product flow throughout the PSC. Both contributions will allow us to formulate research propositions, and identify and discuss opportunities for supply chain improvement in the pharmaceutical industry.

The remainder of this paper is structured as follows. The next section reviews the literature, followed by sections presenting our methodology and interview results. The Discussion summarizes these findings from the perspective of TSEF and provides research propositions. We end with concluding remarks, including suggestions for future research.

2. Literature review

Using a structured literature review approach, this section first highlights the academic and professional literature on the PSC, followed by a review of risk associated with medicine

shortages. Then, TSEF is introduced as a theoretical lens for understanding drug availability and identifying opportunities to improve product flow.

For the literature on PSC, we consulted Google Scholar to look for academic literature and EBSCOHost Business Source Elite to search content in trade publications, using the search strings "pharma supply chain", "pharma supply", "medicine shortage", and "drug shortage". The abstracts of the resulting papers were screened to gain insights about the characteristics of the PSC and the main causes of medicine shortages. Academic papers focusing only on quantitative decision-making in PSCs, not written in English, or not published in journals indexed in the Journal Citation Reports were discarded.

2.1 PSC structure, flows and actors

PSC networks are highly complex, involving hundreds of supply network members (Danese *et al.*, 2006). Specific to the PSC are the primary manufacturers, which produce the Active Pharmaceutical Ingredients (APIs), and the secondary manufacturers which apply further transformations or additions to the APIs to produce the final drugs. Shah (2004) and Rossetti *et al.* (2011) point out that the specialization that the PSC has undergone in recent decades results in a lack of variety and volume flexibility in PSCs. Furthermore, the highly labor-intensive processes in this sector contribute to long lead times of 4–6 months (Keskinocak and Ozkaya, 2020). Moreover, PSC manufacturers tend to have non-dedicated, capacity-constrained production lines where they manufacture different products (Boulaksil and Fransoo, 2010), resulting in complex capacity allocation tasks.

Shuman *et al.* (2020) suggest that manufacturers in the PSC do not maintain a capacity buffer and are therefore unable to meet unexpected increases in demand. Because of this, market fluctuations in the PSC are addressed with inventory buffers. Despite this critical role of inventory, supply chain partners have been pushed to focus on cost efficiency, which led to reductions in inventory levels (Rossetti *et al.*, 2011). This reality limits the overall capacity of the PSC to cope with unexpected events (Woodcock and Wosinska, 2013).

Due to increasing pressure from external financial incentives (Busfield, 2020), PSCs have been pushed to further reduce costs and have adopted outsourcing as one of the main strategic decisions for the primary manufacturing stage (Sweeney, 2020). As a result, most APIs are currently produced in China (60%) and India (Shuman *et al.*, 2020). Although this strategy has resulted in better economic performance, it has reduced the availability of medicines in the EU market (Sweeney, 2020). This is mainly due to overdependence on a few suppliers/countries (Heiskanen *et al.*, 2017; Shuman *et al.*, 2020). This problem is exacerbated by the fact that secondary manufacturing locations tend to be geographically separated from primary manufacturing locations (Shah, 2004).

To ensure that medicines are available at "acceptable" price levels, authorities regulate prices based on several factors, such as an economic evaluation of the drug and income levels (Vogler, 2020). As countries and regions differ with respect to these factors, the outcome of these tools is a price differential across these areas. This market heterogeneity is also distinctly visible among the members of the EU (Vogler, 2020).

2.2 Risk and medicine shortages

According to Van Hoek (2020), there is limited research on how supply chain managers can proactively manage risk. This is particularly true for the PSC due to its specific characteristics and associated vulnerabilities. In this regard, Ward and Hargaden (2019) developed an exploratory risk assessment of the PSC. They suggest that PSCs may be highly vulnerable because they lack flexibility in sourcing, flexibility in order fulfillment, visibility, and collaboration. Furthermore, they identify "connectivity", which is the degree of dependence on external organizations, as the greatest PSC vulnerability in Western Europe.

Jaberidoost *et al.* (2013) conducted a systematic literature review on PSC risk. They found that the most frequent sources of risk were failures to supply the API and regulations, followed

by inventory management issues and counterfeiting. These results are confirmed and extended by Sharma *et al.* (2024) in their investigation of the risks in the Indian pharmaceutical industry, as they found that counterfeiting, demand fluctuations, and poor supplier performance are the main risks present in that industry. Yaroson *et al.* (2023) found that in the presence of long lead times, limited suppliers, and stringent regulations, power-based behaviors negatively impact the effectiveness of reactive strategies. Papalexi *et al.* (2020) study the main causes of operational inefficiency in the PSC of the United Kingdom and Greece by interviewing pharmacy professionals within hospital and community pharmacies. They identify four main causes of inefficiency in the PSC, namely, financial issues, communication issues, waste issues and complexity issues.

One of the most relevant risk effects to study in terms of the operation of PSCs is medicine shortages. An emphasis on efficiency rather than responsiveness has been one of the main drivers for companies to use outsourcing as an effective tool to reduce costs (Rossetti *et al.*, 2011). This lengthening of the supply chain, coupled with limited production capacity and inventory buffers, has made shortages a characteristic of PSCs. Although COVID-19 and its consequences prompted policy makers (Vogler, 2024) and PSC actors (Schleifenheimer and Ivanov, 2024) to develop new methods and strategies for better preparedness, shortages persist within the PSC in the post-COVID period (Biedermann, 2023).

Ahlqvist *et al.* (2023) examine the role of policymakers in employing SC risk management strategies to reduce generic medicine shortages. They compare how seven countries handled shortage risks in their paracetamol (acetaminophen) supply chains before and during the first two waves of COVID-19, concluding that shortages were largely avoided due to implementing multiple strategies prior to the pandemic.

Several studies investigate and categorize the main causes of medicine shortages. Besançon and Chaar (2013) suggest a straightforward classification, dividing the causes into two groups: demand-side and supply-side-related causes. On the demand side, the researchers identify fluctuations in demand, limited purchasing capability, structure of the tendering process and sourcing, and non-traditional demand (exporting/parallel trade) as causes of demand-side shortages. Parallel trade occurs "*when products protected by patent [. . .] are first placed into circulation on one market, then (re-)imported into a second market without the authorization of the original owner of the intellectual property rights*" (Arfwedson, 2004, p. 1).

On the supply side, Besançon and Chaar (2013) list the following causes of disruptions: product discontinuation, availability of raw materials, batch recall, limited manufacturers, low inventory levels, and information management. In addition, drug shortages can also be a consequence of regulatory enforcement actions. Francas *et al.* (2023) analyzed the impact of market, drug substance and level of monitoring on the increased frequency of shortages in the German market. Their findings indicate that higher demand volatility increases the likelihood of a shortage, whereas a higher market concentration and patent protection decrease the likelihood of shortages.

To maintain the quality of medicines, regulators establish and monitor good manufacturing practices (GMPs) (De Weerdt *et al.*, 2015). In the event of non-conformity to GMPs, authorities employ a predefined set of corrective actions, such as recalling all the products from the market or shutting down production sites. Considering product quality as one of the main drivers of recalls, which disturb the flow of products, Ball *et al.* (2018) find that product competition is associated with an increase in recalls with both high severity and low discretion, which may affect product availability for a long period of time.

Several key factors that likely affect product availability in the PSC, as identified in the literature above, can be grouped into a few main underlying causes. First, variability in supply and demand seems to be a leading driver of product unavailability, originating from causes such as parallel trade (Francas *et al.*, 2023), raw material unavailability and product discontinuations (Tucker *et al.*, 2020), batch rejections (Jaberidoost *et al.*, 2013), and unexpected manufacturing stoppages (Besançon and Chaar, 2013). Second, a relatively large number of studies mention production bottlenecks as an overarching cause of product

unavailability in the PSC, including non-dedicated production lines (Boulaksil and Fransoo, 2010); the absence of capacity buffers (Shuman *et al.*, 2020); limited production capacity (Rossetti *et al.*, 2011); and overdependence on only a few qualified suppliers (Heiskanen *et al.*, 2017). Third, non-value-added tasks related to quality non-conformance (Woodcock and Wosinska, 2013), recalls (Ball *et al.*, 2018), and waste issues (Papalexi *et al.*, 2020) are reported to frequently hinder the flow of products. Since supply and demand variability, bottlenecks and non-value-added tasks are all constructs of TSEF (Schmenner and Swink, 1998), we believe it can be used as a theoretical lens to study product availability in the PSC.

2.3 Theory of swift and even flow

The TSEF (Schmenner and Swink, 1998) focuses on explaining the differences in productivity among production units. It states that a quicker and more stable flow of materials through a process results in a more productive process. Therefore, reducing variation and throughput time in any part of the process will result in an increase in productivity (Schmenner, 2015). Furthermore, because throughput time is influenced by variability, due to the Law of Variability (Romero-Silva *et al.*, 2019), a reduction in demand, supply, and process variability will not only result in an even flow, but also in a swifter flow. Schmenner and Swink (1998) further explain that a swift flow is attained by reducing or eliminating non-value-added tasks and by getting rid of process bottlenecks since both cause constraints in the process stages, resulting in an interrupted and uneven flow.

Eltantawy *et al.* (2015) use TSEF to explain the effect of coordination on operational performance in a SC consisting of three independent organizations. They apply TSEF to analyze the flow of both goods and information by identifying bottlenecks and wasteful tasks. In addition, Murat Kristal *et al.* (2010) use TSEF to explain how Quality Management, through the principle of continuous improvement, supports the development of mass customization capabilities by reducing and eliminating variability and defects, resulting in improved flow. Fredendall *et al.* (2009) use TSEF to analyze the flow among the processes in a perioperative surgical service department, attempting to determine how the processes influence the speed and variance of the system flow. Devaraj *et al.* (2013) apply TSEF to the flow of patients in a hospital and conclude that although swift flow affects financial performance, even flow primarily affects quality performance. While TSEF has been used to analyze the flow in various applications, including healthcare, to the best of our knowledge it has not been used in a pharmaceutical context or to directly explain product availability.

Most of the research on PSC has focused exclusively on only a single part of the supply chain (Abdulsalam *et al.*, 2015), on specific pharmaceutical products (Su *et al.*, 2018), and specific therapeutical areas (Tucker *et al.*, 2020). We identify a gap in research spanning across various parts of the supply chain and address it by exploring how drugs move through the different stages of the PSC. Another gap is observed in previous research identifying PSC risks and causes of shortages without explicitly considering their relationship with product flow. We contribute to closing this gap by adopting TSEF as a theoretical lens, similar to Fredendall *et al.* (2009), in order to identify which factors hinder the swift and even flow of products, thereby threatening drug availability. We specifically map PSC processes, policies, and actors to identify sources of variability, bottlenecks, and non-value-added tasks. The categorization of phenomena that could hinder the swift and even flow of drugs allows us to understand and analyze their potential impact on drug availability and to formulate research propositions for future research.

3. Methodology

3.1 Research setting

The Netherlands has a population of 17.5 million as of July 2021 (Centraal Bureau voor Statistiek, 2021). Health insurance in the Netherlands is mandatory (van de Ven and Schut,

2008), with pharmaceutical expenses per person being among the lowest in Europe (OECD, 2020).

The pharmaceutical sector in the Netherlands is highly regulated. Prices of individual drugs are bound by law (Farmatec, 2020) and reimbursement by basic health insurance is limited to products listed in the drug reimbursement system (Rijksoverheid, 2020). Generic drugs sold in public pharmacies are tendered by a number of health insurance companies covering the majority of the Dutch population. When a patient needs a certain drug (molecule), they should receive the label *their* insurance selected, and not any of the other equivalent labels that the pharmacy also stocks. This is called a preference policy (KNMP, 2020). Hospital pharmacies are not bound by the preference policy, but are instead united in procurement groups.

In recent years, Dutch PSCs exhibited challenges in terms of medicine availability. In 2018, the Netherlands recorded shortages of 750 different drugs, followed by almost 1,500 shortages in both 2019 and 2020 (KNMP, 2019a). Additionally, the government requires manufacturers to report both shortages and expected shortages (Inspectie Gezondheidszorg en Jeugd, 2020). The Dutch Ministry of Health, Welfare and Sport is exploring ways to reduce shortages, such as imposing minimum stock requirements (Tweede Kamer, 2020). All of the above signals that the Netherlands is facing difficulties in terms of pharmaceutical product availability. The flow of products may be affected by the large number of actors involved in the SC and the many regulations. Therefore, we consider the Dutch PSC an appropriate setting to examine medicine availability from the perspective of swift and even flow.

The above laws and policies apply to the Dutch market but other countries are adopting similar practices. The Dutch process of tendering per insurance company is rather unique in Europe, with only Germany having a similar system (IQVIA, 2020). However, Canada recently started to tender drugs on a province-by-province basis (Reguly *et al.*, 2021). Another example is the 1996 Dutch price law that bounds drug prices by the average price in a few other countries. These countries are called the *reference basket*, and it is updated regularly to ensure that it includes countries with low prices. This concept is internationally known as External Reference Pricing (ERP) (Iravani *et al.*, 2020). Currently almost all European countries use ERP (Rémuzat *et al.*, 2015).

The complexity of the Dutch PSC makes it difficult to study the causes of drug shortages across the entire supply chain. We believe that TSEF (Schmenner and Swink, 1998) can help us overcome this issue because of its focus on product flow. TSEF is typically applied at the firm level (Devaraj *et al.*, 2013; Fredendall *et al.*, 2009), but we believe it is an appropriate theoretical lens to examine product flow throughout the entire value chain. Thus, we use this theory to dissect the PSC, structure the insights gathered from industry experts (as opposed to most of the literature on drug shortages (Tucker *et al.*, 2020)), and identify the sources impacting the flow of goods, which ultimately affects product availability. Similar to Bhakoo and Choi (2013), who use institutional theory to understand institutional pressures in the healthcare supply chain, we use TSEF to formulate propositions to guide future research on the relationship between PSC operating environments and drug availability.

3.2 Scope

Due to the large number of drugs in the Dutch PSC, the research scope was narrowed down by classifying pharmaceutical products. In practice, pharmaceutical products are classified in different ways, for example (1) commercial trade vs. pharmacy preparation, (2) inpatient (hospital) vs. outpatient (e.g., pharmacy, drugstore), or (3) prescription vs. over-the-counter drugs. Another classification distinguishes between generic or innovative medicines, “orphan”, biological medicines, and vaccines.

Because we expect product flow to be affected by the way a supply chain is organized, and want to control complexity, we use the well-known supply chain strategy framework of Lee (2002) to classify pharmaceutical products. The framework of Lee (2002) matches the classification of drugs according to generic and innovative medicines.

Generic or off-patent drugs typically face different market conditions than patented drugs. As off-patent drugs face competition from generic manufacturers, they exhibit lower profit margins and demand uncertainty, whereas patented drugs can be considered innovative products characterized by higher margins and higher levels of demand uncertainty. The production technology for chemically synthesized drugs is generally well established; the technology for biologicals is more complex as it involves creating products from living cells (Morrow and Felcone, 2004). Examples of biologicals include antibodies, insulin, and enzymes. In Lee's framework (2002), the production of chemically synthesized drugs would be labeled as stable, and thus exhibiting low levels of supply uncertainty. The production technology of biologicals could be described as evolving, and therefore exhibiting higher levels of supply uncertainty.

We classify pharmaceutical products in Table 1. The middle column contains all products that are currently off-patent. Such a product can be produced either by the original manufacturer or by others. These variants from other manufacturers are called generics (for chemically synthesized drugs) or biosimilars (for biological drugs). In the rightmost column, products are called specialty drugs (the chemically synthesized ones) and biologicals.

Following Lee (2002), different levels of supply and demand uncertainty need to be met by different supply chain strategies, as indicated in Table 1. By studying products with varying characteristics in terms of market, regulations, and technological processes, we aim to understand how different PSC structures, vulnerabilities, and dependencies affect product flow within the industry.

As the Dutch PSC displayed challenges in terms of medicine availability in previous years (KNMP, 2019b), the research focused on the structure, dependencies and vulnerabilities in the Dutch PSC that existed prior to COVID-19.

3.3 Data collection approach

A qualitative exploratory study is appropriate, as our aim is to gather information and perspectives on the structure and operations within the Dutch PSC. By examining the PSC from the perspective of a single country, we control for the influence of national regulatory aspects within a global network. We use a multiple case study approach, supported by structured interviews. Collecting evidence from multiple cases is an established method to make the results robust (cf. Yin (2013)).

Prior to the interviews, we held preparatory meetings with national industry associations. This included meetings with two drug manufacturing associations: *VIG* (VIG, 2020) for innovative drugs and *BOGIN* (BOGIN, 2020) for biosimilars and generic drugs. We also spoke with the wholesalers' organization *BGPharma* (BGPharma, 2020), the public pharmacists' (PHs) organization KNMP, a hospital pharmacist, a manufacturer and a wholesaler organization.

We interviewed experts from different echelons until we reached theoretical saturation, where many of the themes discussed by the interviewees were being reiterated and no new insights were being provided. We interviewed eight PHs, referred to as PH1–PH8. We aimed for a varied selection by including public, hospital and university hospital pharmacies. We also

Table 1. Classification of pharmaceutical products and supply chain strategies

	Off-patent	Patent protected
Chemically synthesized	efficient	responsive
Biological	risk-hedging	agile

Source(s): Authors' own work

interviewed two leading wholesalers (W1, W2) and four manufacturers (M1–M4), consisting of a mixture of generic and patented manufacturers. Interviewees were informed of the nature of the interview in advance and could invite colleagues with complementary expertise, which several interviewees did. A summary table and coding related to the interviewees can be found in the "Overview of interviewees" section in the Supplement.

We used a semi-structured interview format with open-ended questions for the interviews. This enabled us to follow the same procedure for the interviewees in each echelon and gather consistent information throughout. All interviews were conducted via 60-min video calls.

The interview protocols for the PHs, wholesalers and manufacturers are found in the Supplement with corresponding names. To avoid potential bias in interpretation, at least two interviewers participated in each interview and took detailed notes, which were sent back to the interviewees for validation. After the research team processed the feedback, the team analyzed the resulting interview notes on a sentence-by-sentence basis. To avoid potential bias in the analysis, one of the authors conducted an initial assessment and other authors subsequently verified the analysis and interpretation of the identified results. First, an open coding approach was used to identify a total of 153 relevant quotes in the transcribed interviews. A subsequent axial coding stage led to the identification of 26 unique risk and vulnerability drivers, each of which was cross-validated with the risk and vulnerability drivers that are reported in the generic risk frameworks by Pettit *et al*. (2013), Ho *et al*. (2015), and Hosseini *et al*. (2019). The final selective coding stage resulted in the classification of the risk and vulnerability drivers into five core categories, which relate to the different operating environments of the PSC. The mapping of drivers and operating environments along with the constructs of TSEF were then used to structure our results and define the propositions of the study. Figure 1 illustrates the research design of this study, including the steps explained in Section 3.

4. Results

We have adopted the SC visualization of Hansen and Grunow (2015) to envision the PSC network. Based on the interviews with different Dutch PSC actors, we included raw material suppliers, excipient manufacturers, pre-wholesalers, and distinct "markets" such as hospitals, (public) pharmacies, patients, and other markets. We reduced the level of detail for the secondary production stage by removing packaging and blistering from the Hansen and Grunow (2015) framework.

Figure 2 gives a general overview of the PSC structure that supplies the Dutch market. The rectangles represent a transformation of materials and the triangles represent product storage. The structure, dependencies, and vulnerabilities in the PSC are explained in more detail in the following subsections.

The interviewees confirmed the overall structure of the PSC depicted in Figure 2, indicating that the simplified model is basically correct (M3) [1], and that it probably covers 99% of the volume in the Dutch market (M1). The PSC typically starts with the production of raw materials. *Raw material suppliers* supply several industries, including the *API manufacturers* and *excipient manufacturers* of the pharmaceutical industry. While raw materials can be supplied by several parties, the number of API manufacturers is limited. For some APIs, there are only a few (sometimes only 1 or 2) manufacturers available worldwide, as many smaller API manufacturers have disappeared from the market over the past decade. Even if an alternative API manufacturer is available, it is not easy for a drug *manufacturer* to switch suppliers: it requires re-registration of the product, which takes a significant amount of time and effort.

Manufacturers typically maintain stocks of finished products, which they store at *pre-wholesalers*. The pre-wholesaler is not the owner of the product (manufacturers are the owners; consignment stock) but keeps safety stock and supplies wholesalers and possibly other parties. *Wholesalers* keep an inventory of drugs and aim to meet the demand that arises in a country. Wholesalers in the Dutch PSC receive supplies either from a pre-wholesaler or from

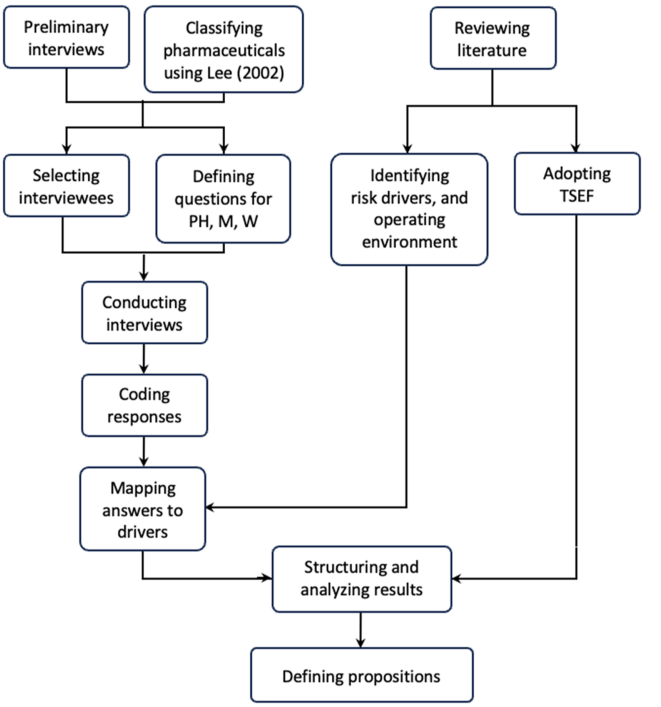

Figure 1. Research design. Source: Authors' own work

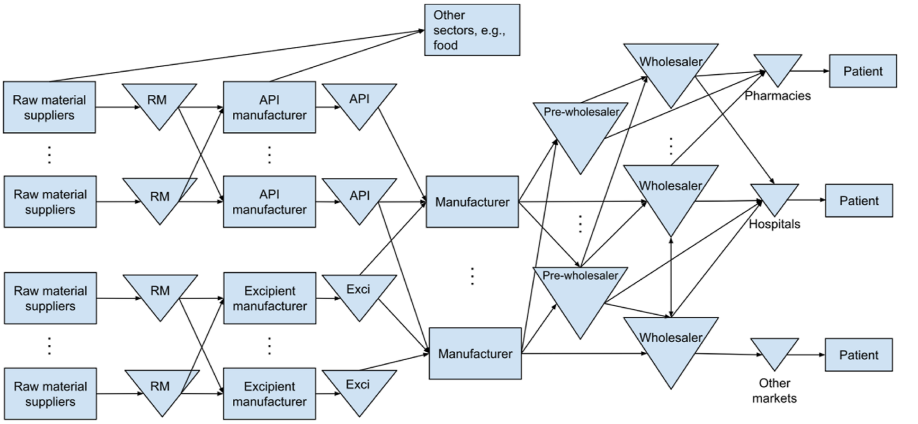

Figure 2. Pharmaceutical supply chain delivering to the Dutch market. Source: Authors' own work

a manufacturer's warehouse in the Netherlands or elsewhere in Europe. The Dutch market has four leading wholesalers that carry almost identical drug portfolios, supplying to pharmacies, hospital pharmacies or self-dispensing physicians. In the Netherlands, wholesalers cannot supply directly to a patient; all drugs must go through a pharmacy. Figure 2 illustrates how patients can obtain drugs from a *public pharmacy* or a *hospital pharmacy* as a part of their treatment. PHs and hospital PHs dispense different products. For example, most biologicals

are handled by hospital PHs and not by public pharmacies. Public pharmacies place their orders with a single distributor (wholesaler).

4.1 Risk and vulnerabilities

This section highlights the main characteristics of the Dutch PSC that the interviewees identified as having an impact on drug availability. We applied the approach visualized in Figure 1 to construct Table 2. This table summarizes key risk drivers reported by several supply chain actors (M: manufacturers, W: wholesalers, PH: pharmacists), some of which directly relate to the TSEF. The drivers are categorized into several operating environments: (1) manufacturing and SC processes; (2) competitive environment; (3) information transparency;

Table 2. Summary of Dutch PSC characteristics

Vulnerability or risk	M	W	PH
(i) Manufacturing and SC processes			
a. Single sourcing of raw materials (including "molecules") and/or lack of alternative raw material suppliers	✓	✓	✓
b. Panic buying or stockpiling by patients or pharmacies	✓		✓
c. Lack of redundancy in production capacity	✓	✓	
d. Geographic concentration of suppliers			✓
e. Long lead times	✓		✓
f. Inability of manufacturers to react swiftly to changes in demand and demand forecasts	✓		✓
g. Inability of parallel traders to react quickly to shortages	✓		
(ii) Competitive environment			
a. Competition for raw materials with other industries, especially the food industry	✓		
b. Consolidation of manufacturers and/or lack of alternative suppliers	✓	✓	✓
c. Lack of facilities, knowledge, and expertise to reshore raw material production	✓		
(iii) Information transparency			
a. Lack of transparency about inventory levels and import /export volumes among manufacturers and between manufacturers and wholesalers	✓	✓	
b. Lack of transparency and control of (conditions at) raw material supplier	✓	✓	✓
c. Lack of transparency and control of supply and demand volumes due to parallel trade	✓	✓	✓
d. Lack of good systems to monitor drug availability and automated ordering processes between manufacturer and wholesaler	✓		✓
e. Lack of information transparency between pharmacy and manufacturer/wholesaler about prices, volumes, and source of raw materials			✓
(iv) Regulatory environment			
a. Frequently renewed tenders	✓	✓	✓
b. Complex and expensive procedures regarding the use of "shared pack" boxes and multilingual boxes/leaflets	✓	✓	✓
c. Frequent price law recalibrations	✓	✓	✓
d. Complex, un-harmonized, and expensive registration processes among EU member states for new and existing drugs	✓		✓
e. Differences in legal (quality) requirements for the same ingredients by the over-the-counter (OTC) board, European Medicines Agency (EMA) board, and food industry	✓	✓	
f. High costs of (complying with) complex legal policies	✓		✓
g. Long external quality and safety testing procedures	✓		
h. Requirement to have multiple quality tests of the same production batch for different shipments		✓	
(v) Product characteristics			
a. Inflexibility in demand due to medical reasons and bureaucracy		✓	✓
b. Contamination and quality risks	✓	✓	✓
c. Operational complexity of the drug production process	✓	✓	✓

Source(s): Authors' own work

(4) regulatory environment, and (5) product characteristics. The check marks indicate whether a concern was expressed by at least one interviewee among each supply chain actor.

The concerns expressed by the interviewees are structured according to the operating environment in Table 2. The most frequently mentioned concerns regarding product availability in the PSC relate to vulnerability factors related to resource limits and external pressures (Ho *et al.*, 2015). Specifically, the risk drivers that are identified from these concerns mostly relate to supply inflexibility, such as the inability to switch between manufacturers due to contractual obligations. Other risk drivers include the impact of government policy and regulation, the lack of additional stock and redundancy in inventory, price pressures, and challenges related to production-ordering policy. Interviewees from at least two out of the reported three echelons expressed concerns that could be related to any one of these factors. Table 2 does not take into account interviewees' beliefs about relative importance, nor does it distinguish between causes and effects. The next several sections elaborate on the interview findings with regard to vulnerability and risk in the PSC.

4.2 Manufacturing and supply chain processes

Interviewees observed that generic drugs in the Dutch PSC are manufactured by only a few manufacturers - typically in India and China. Biologicals are more commonly produced in Western countries (PH1). The sources and form (generic or biological) of drugs influence production capacities, lead times, production process, and supply chain planning horizon.

Production capacity is a significant challenge for the PSC. W2 observes that generic supply chains operate at maximum capacity, so any disruption will lead to problems. Leading manufacturers sometimes operate at 103% capacity utilization in order to produce at, say, 22 cents a box, which they can deliver to the Dutch market for 25 cents. To illustrate the difficult situation generics manufacturers are in, W2 contrasts this with the 60–70% capacity utilization that originators employ. Having fewer generic drug manufacturers in the market operating at high utilization rates increases vulnerability and reduces supply chain resilience. M3 illustrates this with the example of one of its European factories that was forced to close due to COVID-19. According to M3, it took a long time to recover and produce the entire backlog, especially since the plant was already operating at over 90% utilization.

Estimates of *lead times* for the Dutch PSC vary widely among the interviewees, depending on the origin of the materials and the specific product concerned. EU-based manufacturers sourcing APIs from India often face lead times of six to seven months (M1). However, due to fairly stable ordering and replenishment processes, little to no safety stock is held for APIs. Another related challenge is the use of *batch production.* M2 indicates that if one had to start production for one of their products from scratch, it would take three months to get a final product. Large production batches are common due to significant changeover costs.

M4 has a *supply chain planning horizon* of 6–18 months; one to six months of production is more or less locked in. The company distinguishes between life-saving drugs and those which are not, and examines whether competitors have alternatives. Critical products are given priority in terms of production and delivery.

On average, the interviewed manufacturers keep about four months of sales in stock at the pre-wholesaler for the Dutch market. However, stock levels vary from product to product and typically depend on the criticality and shelf life of the product. In addition to wholesaler stock, M4 stores additional language-neutral packaging at its production sites.

4.3 Competitive environment

Tight margins in this sector have pushed actors in different echelons of the PSC to focus on *cost efficiency,* resulting in mergers of both API manufacturers and drug manufacturers over the past decade. According to several respondents, there used to be five to seven producers for a given drug, but now there are only a few. Economies of scale have also been pursued

downstream, with Dutch pharmacies consolidating in response to lower margins. Competitive pressures in the PSC extend to *shared raw materials markets*, as raw material and API manufacturers allocate some of their production capacity to other industries, such as the food supply chain.

4.4 Information transparency

Interviewees criticize the lack of information transparency in *raw material production*, making it difficult to predict or trace the origin of contaminations. Several respondents also identify *unknown inventory levels and flows* throughout the PSC as a barrier to effective planning. Information on available inventory at different echelons, canceled or delayed replenishments, and import and export volumes is believed to help other players of the PSC to anticipate disturbances in the supply chain.

4.5 Regulatory environment

According to interviewees, the supply chain of generic drugs witnessed a major change in 2008 after the introduction of the preference policy by the Dutch government. This allows health insurance companies to regularly tender off-patent drugs to competing manufacturers. The result is, for each drug, the selection of a "preferred" label that is binding for the patients of that health insurance company. This implies that, at each point in time, the different echelons in the supply chain must hold sufficient stock of all currently preferred labels.

There are at least 10 competing health insurance companies in the Netherlands (Ministerie van Volksgezondheid, 2018) who regularly tender for preferred drugs. This makes it very difficult for supply chain partners to ensure supply continuity. In fact, the identification of preferred drugs forces supply chain partners to stock products at the level of specific brands (preferred by some health insurance companies) instead of at the level of active substances in order to ensure drug availability. Disaggregating the demand for an active substance into a demand for a variety of specific labels containing the same active substance increases the overall demand variability for the supply chain. Moreover, manufacturers tend to decrease the stock of a product that may lose preference in the future, while the new preferred manufacturer has minimal time to ramp up production. Furthermore, shortages are also observed in anticipation of the *expiration of patents*. When patents expire, generics or biosimilars are immediately available and prices can drop by 90–95%. As a result, some manufacturers choose to ramp down production before the patent expires.

Temporary shortages are sometimes related to *parallel trade*. Import and export relationships may change suddenly, which can lead to oversupply or undersupply. Another factor that can have a significant impact on import and export is changes in *government-imposed prices*. When an update to the ERP reference basket is announced, it is possible to determine which products will experience a price decrease, and PSC actors decrease their stock levels of these products accordingly, even before the update takes effect. To reduce import and export flows, manufacturers can decide to sell only a limited amount to each wholesaler by setting *quotas* based on patient demand data. Quotas can lead to shortages because if a wholesaler has additional demand, it can take several months for the manufacturer to adjust the replenishment quantities.

The government intervenes in the market by imposing the following *supply regulations*. Manufacturers are obliged to signal changes in their product availability 3 months in advance. M1 recounts how a 7-month supply of a product (under normal use, for their regular market share) lasted only 1 month after all competitors ran out of stock. As a result, they were fined for reporting the impending shortage too late. Besides reporting, manufacturers are expected to respond quickly to changes in demand and supply. Every marketing authorization holder is obliged to supply the entire market "sufficiently" (Geneesmiddelenwet, 2020 Art 49 part 9), *regardless of their market share*, and failing to do so risks a fine of up to € 800,000 (M3). Finally, M3 observes that new regulations have

shortened the shelf life of products to a maximum of 24 months, which adds to the challenge of matching supply and demand.

EU import *testing* is done at the shipment batch level, not the production batch level. Since many products can only be tested at one lab in Europe, these labs are often too busy to test immediately. Although testing generally takes two weeks (M1), it can sometimes take four to six weeks (M3).

EU *safety and environment* laws have likewise become stricter over time, making offshoring production a financially attractive option. M1 points out that if India and China were to adopt the same safety and environmental measures, then it would become less financially attractive to produce there.

4.6 Product characteristics

Several interviewees indicated that the *category with the most shortages* is in the upper left quadrant of Table 1 (chemically synthesized, off-patent) and that very few shortages occur for patented drugs. The high margins in this category were mentioned as a possible reason.

The production of biologicals involves a much more *complex supply chain* than chemically synthesized drugs. It involves living organisms for which production cannot be accelerated. The active ingredient sometimes has to go through as many as 17 different production sites (W2).

The product categories also differ in terms of *demand characteristics and market alternatives*. Chemically synthesized drugs are typically tendered by insurance companies through the preference policy. Their preference for a certain label is binding and, as a result, the Dutch market is not financially attractive for manufacturers whose drugs are not preferred. In contrast, the preferred label for biologicals is typically decided by hospital procurement groups, and prescribing their label of choice is *not* strictly enforced. This maintains a market for the alternatives and, as a result, the manufacturers keep these alternative drugs approved/licensed for sale in the Netherlands. PH4 speculates that this may explain why hospitals do not face shortages of biologicals.

5. Discussion

This section discusses how operating environments, their key constituting risk drivers, and interactions can influence product availability. Using TSEF as a theoretical lens, we examine how drug flows and availability are affected. In this regard, we draw on TSEF by identifying sources of variability, bottlenecks and non-value-added tasks that may interrupt the flow of drugs in the PSC (see section 6 in the Supplement for a visualization of the identified relationships). Based on this analysis, we also formulate three propositions to explain the effect of PSCs operating environments on drug availability that could serve as motivation for future research.

5.1 Propositions

5.1.1 Variability. TSEF states that productivity can increase if materials flow more evenly, for example by lowering the variability of demand or the variability in the production processes. As such, TSEF identifies the harmful consequences of variability on productivity.

Interviewees across the supply chain identified a large number of drivers that contribute to an increased variability in demand for specific drugs, variability in process operations and product specifications. Although demand for generic drugs at the molecule level is often quite stable over time, several factors in the regulatory environment category cause demand at the individual drug label level to fluctuate significantly. The most frequently cited cause is the tendering to assign preferred drugs. Not only the frequency of the tenders (mainly once every two years, M3[22]), but also the number of actors that conduct tenders (health insurance companies and wholesalers) increases demand variability, requiring supply chain actors to

quickly decrease or increase production and inventory levels for specific labels. On the one hand, as mentioned by W2[21] and PH3[22], manufacturers already start decreasing the stock of a product that may lose preference in the future. On the other hand, a new preferred party has little time to ramp up production in time to have sufficient inventory available (W1[23], W2 [21]). Tendering (as a source of variability) occurs uniquely for off-patent drugs, and mostly for those that are off-patent chemically synthesized.

One exception, however, where demand surged for certain molecules, occurred during the first wave of COVID-19. Hospital PHs experienced an unprecedented demand for drugs used to sedate patients in the intensive care unit (PH5[24]), and public PHs observed hoarding behavior for paracetamol (PH3[25]). When demand suddenly surged, manufacturers of generic drugs had little flexibility to respond, which led directly to product shortages.

Demand fluctuations are also triggered by changes in product price and product status. Updates of the price law and expiring patents imply an expected price drop and cause parties throughout the PSC to reduce their inventory in anticipation (M2[26], W1[27], W2[28], PH6 [26]). Moreover, changes in parallel trade directly affect required production levels and can suddenly change product flows within the production distribution networks (M2[30], M3 [31]). This is compounded by a manufacturer's obligation to supply the entire market regardless of its original market share.

The challenging competitive environment for off-patent drugs and resulting increased focus on cost efficiency has resulted in producing larger batches (PH1[32], M3[33]), thereby increasing variability in shipment quantities and cycle stocks. This effect is amplified by quality (contamination) (M1[16, 34]) and availability issues (competition with other industries) in the supply chain (M1[35]), long lead times (M1[7], M3[36]), and the decreasing number of suppliers and manufacturers due to consolidation in the industry (M3 [37], PH5[38], PH6[39]).

An additional challenge is the fact that information sharing in the PSC is limited. Only manufacturers are obliged to report anticipated shortages for the Dutch market, but (expected) shortages at wholesalers and parallel traders can also lead to severe disruptions of product flow in the SC (PH5[40]). To the best of our knowledge, no other demand- or inventory-related information is structurally shared with regulators and/or SC actors.

The pharmaceutical market is segmented by country or region, resulting in missed opportunities for processing similar products together. For example, drugs are packaged for individual countries or regions and can differ in dose, leaflet language and product name (M2 [41], W1[42]). This is an additional source of variability that not only affects production but also misses opportunities for inventory pooling. When drugs originally packaged for one country are imported by another country, they need to be repackaged (see non-value-added tasks), which could be avoided by using more "shared packs" (W4[43], PH3[44]). Based on these observations, we propose:

P1. Variability caused by the regulatory environment and the competitive environment has a negative influence on manufacturing and supply chain processes, thereby reducing drug availability in PSCs.

5.1.2 Non-value-added tasks. Non-value-added tasks are activities that consume resources but do not add value to the product. According to Schmenner and Swink's definition of a non-value-added task (see Schmenner and Swink, 1998, p. 102), there are various activities in the PSC that are important but do not necessarily add value to the product. For example, frequent testing (i.e., quality inspections) per shipment batch increases lead time by 2–6 weeks (M1 [16], M3[17]). Although quality inspections play a crucial role in ensuring drug safety, the task itself is technically non-value-added if it is only intended to compensate for potential shortcomings in a production process. As a result, inspections are not considered part of value-added operating time (Slack *et al.*, 2022, p. 373). The uncertainty associated with the increase in lead time and the risk of rejection has a direct impact on product availability. Similarly, parallel trade plays a role in redistributing drugs to better fulfill national demands. However,

parallel trade requires additional transportation and repackaging, which are also non-value-added activities. Similarly, several other essential tasks in the PSC can be considered to be non-value added, including product (re-)registration, monitoring drug shortages, and transportation.

Although certain processes, such as inspection, are required by law, TSEF draws attention to the fact that other non-value-added tasks exist in the PSC, resulting in increased throughput time, cost and inefficiencies. Therefore, we propose:

P2. Non-value-added tasks due to the regulatory environment have a negative influence on manufacturing and supply chain processes by increasing variability and throughput time, thereby reducing drug availability in PSCs.

5.1.3 Bottlenecks. Bottlenecks impose a constraint in the productivity of a process by interrupting the flow of goods (Schmenner and Swink, 1998). Global PSCs share suppliers of raw materials with other industries. In addition, there are a limited number of excipient and API manufacturers due to a focus on cost efficiency, creating a significant bottleneck in the early stages of PSCs.

This reality is particularly evident for off-patent, chemically synthesized drugs, where pricing laws and tendering practices, which are part of the regulatory environment (see section 4.5), have pushed the pharmaceutical industry to limit investments in manufacturing capacity and working capital, resulting in large production batches and high-capacity utilization. High-capacity utilization, in turn, hinders the flexibility of PSCs and their resilience to face uncertainties. These findings from the interviews are consistent with previous studies on drug shortages (Cockburn, 2004; Rossetti *et al.*, 2011; Shah, 2004). Similarly, bottlenecks might also arise in the Dutch PSC if one of the "preferred" manufacturers experiences a stoppage, as there are only a few manufacturers supplying the market for some drugs, as confirmed by the Dutch drug manufacturing association VIG (Biedermann, 2022).

While for some diseases several drugs are available on the market, the possibilities for demand substitution are sometimes limited for medical reasons. This is confirmed by external sources, such as for thyroid patients (AVRO Tros, 2021). In 2021 the Medicines Evaluation Board (CBG) published the list "Switching undesirable" (CBG, 2021) and offered it to the Dutch Ministry of Health, Welfare and Sport. Moreover, most Dutch health insurance companies further restrict the demand substitution of drugs by reimbursing only their specified label of preference.

When manufacturers impose delivery quotas to countries or regions to limit parallel trade and ensure sufficient supply to national markets or wholesalers, they constrain the flow of products, resulting in delays in drug availability, see for example AVRO Tros (2019). Further, the effect of inventory constraints on product availability is compounded by a lack of information transparency in the PSC, as manufacturers and wholesalers are not able to quickly react to sudden changes in national demands and inventory availability. This phenomenon highlights how various factors affecting different stages of the PSC interact to negatively influence drug availability downstream. Based on these observations, we propose:

P3. The regulatory environment, competitive environment, and the lack of information transparency create bottlenecks in PSC manufacturing and supply chain processes, thereby reducing drug availability.

5.2 Integrative framework explaining drug availability

Based on Propositions 1, 2, and 3, we construct an integrative framework that explains the inhibitors of drug availability presented in Figure 3. This framework illustrates that the competitive environment and lack of information transparency only affect the TSEF constructs of variability and bottlenecks, which in turn influence manufacturing and supply chain processes, and ultimately has an effect on drug availability. The regulatory environment, however, influences all three constructs of TSEF, including non-value-added tasks.

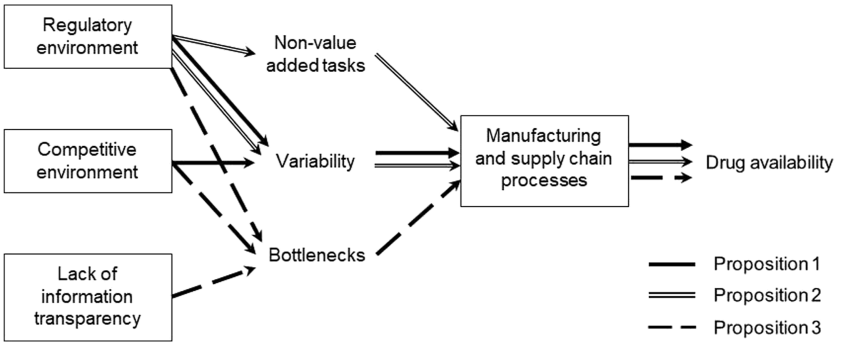

Figure 3. Integrative research framework (operating environments shown in boxes). Source: Authors' own work

This framework integrates operating environments affecting product flow in PSCs to support further research on drug shortages. For instance, researchers and practitioners could use this framework to investigate how new regulations could impact drug availability. Prescriptive research could also, for example, investigate how increased information sharing along the PSC allows better management of bottlenecks to reduce shortages.

5.3 Theoretical implications

This study contributes to the literature on PSCs by offering new insights to the main inhibitors influencing drug availability. Increasing competitive pressure in the pharmaceutical industry, especially for generic drugs, has caused manufacturers to focus on cost efficiency (Rossetti *et al*., 2011), to no longer maintain capacity buffers (Shuman *et al*., 2020) and to increasingly adopt outsourcing to Asia (Shuman *et al*., 2020). Other studies such as Sweeney (2020) suggest that these practices have reduced the availability of medicines in the EU market. Ball *et al*. (2018) identified a causal link between increasing competitive pressures and higher number of recalls due to a decrease in quality standards, which could be considered indirect evidence related to Proposition 1. The proposition as formulated in this study, however, offers a more encompassing explanation for the underlying mechanisms causing reduced drug availability.

Legislation related to quality non-conformance (Woodcock and Wosinska, 2013), recalls (Ball *et al*., 2018), and waste issues (Papalexi *et al*., 2020) can affect the flow of products that subsequently creates inconsistencies in drug availability. Proposition 2 sheds light on the drivers behind the interaction between such non-value-added tasks and drug availability.

Manufacturing and supply chain constraints often contribute to the creation of bottlenecks, including capacity-constrained production lines (Boulaksil and Fransoo, 2010); the absence of capacity buffers (Shuman *et al*., 2020); and overdependence on only a few qualified suppliers (Heiskanen *et al*., 2017). Proposition 3 provides additional perspective to these theoretical insights by pinpointing how specific phenomena from three different operating environments cause these practices to exacerbate drug shortages.

5.4 Managerial implications

The results of this study offer insights to regulators, policy makers and PSC actors. Although there is ample literature discussing the reasons and ways in which authorities regulate drug prices (Vogler, 2020) and some research has tried to understand the effects of regulations on the performance of PSCs (see, e.g., Chen *et al*., 2020; Dobrzykowski, 2019), our study is the first to emphasize the influence that such interventions have on *variability* in the supply chain. Proposition 1 encourages industry associations of manufacturers, wholesalers, PHs and policy makers to consider the unintended side effects that increasing regulatory and competitive pressures have on *product availability.*

The influence of non-value-added tasks stemming from regulatory measures on throughput time in the PSC has been extensively described in the literature (see, e.g., Abideen and Mohamad, 2020; Al-Araidah *et al*., 2010). Our findings also show the vital role of variability in establishing this relationship. We therefore especially call on regulatory agencies, parallel traders and manufacturers to reevaluate the effectiveness of current mitigation strategies to reduce variability originating from non-value-added tasks. For example, re-assessing the conditions under which parallel trade after batch rejection enhances or diminishes drug shortages through variability and throughput times can lead to more specific policies to improve product availability in the PSC. Reducing non-value-added tasks created by the regulatory environment is particularly important in critical circumstances such as the one faced in COVID-19 as non-value-added tasks might lengthen throughput times when instead the flow needs to be swifter.

Practitioners and policy makers can take advantage of the insights generated in this study to mitigate bottlenecks by re-evaluating the impact of price law changes and tender frequencies on drug shortages or by enhancing information transparency. In this regard, it can be worthwhile to study successful implementations of transparency enhancing technologies from related industries, such as the use of blockchain and artificial intelligence in agri-food supply chains (El Bhilat *et al.*, 2024).

6. Conclusions

PSCs are complex supply chain networks involving private and public supply chain actors that participate in the acquisition, production and delivery of raw materials, intermediates, and finished products to markets. The COVID-19 pandemic triggered additional and reinforced existing product shortages and emphasized the importance of understanding risk drivers in the supply chain.

In contrast to previous studies that focus on the *performance (productivity)* of actors of specific products or processes in a single stage of the PSC and do not explicitly relate causes of shortages to product flow, this paper examines the main inhibitors that limit product flow across different stages of the PSC and their impact on product availability. Our theoretical contribution lies in demonstrating how TSEF (Schmenner and Swink, 1998) can be adopted as a theoretical lens to study product flow beyond a single company or supply chain echelon. Extending its scope to multiple stages of an entire supply chain allows us to structure and analyze drivers for product availability through each of its tenets. This study extracts and structures the findings from expert interviews along the three main TSEF tenets that inhibit the stability and speed of product flow of PSCs: variability, bottlenecks and non-value-added tasks.

Most drivers of drug shortages identified by interviewees are related to variability. Moreover, drivers related to variability are mentioned several times independently by different actors, highlighting the major role that variability plays in the availability of drugs. It is specifically worth mentioning that several sources of variability are related to the organization of the downstream supply chain stages. For example, various countries have introduced policies to lower drug prices. Although they have been rather successful in achieving this objective, some measures had the unintended side effect of introducing variability that was not inherently present in the market. Since several risk drivers belong to the regulatory environment, a reality that PSCs share with the healthcare industry (Dobrzykowski, 2019), policymakers are encouraged to be more aware of their impact on variability, bottlenecks, and non-value-added tasks that may affect product availability.

Our practical contributions lie in the interpretation of these results, which led to the formulation of three propositions, one for each of TSEF's tenets. Hence, we were able to conjecture on the interactions between relevant factors influencing product availability and how product availability is hindered throughout multiple stages of a supply chain. Our practical advice centers around identifying measures and practices that TSEF's tenets highlighted as having unintended side effects, while also warning of possible future ones.

6.1 Limitations and future research directions

One limitation of this study is that it only involves supply chain actors producing and moving drugs. In addition, although the Dutch setting is a good illustration of a complex network of supply chain actors and governance mechanisms, their influence on product flow and drug availability might differ across countries. Therefore, future research could consider the perspective of these additional stakeholders (e.g., API and excipient manufacturers, and regulators and policymakers) and the national characteristics of operating environments when validating or extending the proposed integrative framework.

Future research could also empirically test our research propositions using survey data from the various echelons examined in our study of PSCs, as well as other industries where the regulatory environment has a significant impact on product flow. Moreover, it could be interesting to quantify the relative impact of each TSEF construct on the overall performance of the PSC.

In addition, future research could investigate the impact of interviewee suggestions to reduce shortages. We highlight a few that are related to TSEF: (1) prohibiting parallel trade, (2) reducing the frequency of drug tenders by insurance companies; and (3) introducing a "direct to patient" model where drugs bypass the pharmacy echelon. These require further study as their adoption poses potential challenges, such as (1) fewer options to redistribute drugs (2) increased prices, and (3) reduced PHs' ability to monitor pharmacological interactions that can adversely affect patient safety.

Notes

1. From now on, this is how we quote individual interviewees. The codes can be looked *p* in section 1 of the Supplement "Interview Protocol".

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Supplementary material

The supplementary material for this article can be found online.

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