ECONOMICS

Adapting to disruptions: Managing supply chain resilience through product rerouting

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Supply chain disruptions may cause shortages of essential goods, affecting millions of individuals. We propose a perspective to address this problem via reroute flexibility. This is the ability to substitute and reroute products along existing pathways, hence without requiring the creation of new connections. To showcase the potential of this approach, we examine the US opioid distribution system. We reconstruct over 40 billion distribution routes and quantify the effectiveness of reroute flexibility in mitigating shortages. We demonstrate that flexibility (i) reduces the severity of shortages and (ii) delays the time until they become critical. Moreover, our findings reveal that while increased flexibility alleviates shortages, it comes at the cost of increased complexity: We demonstrate that reroute flexibility increases alternative path usage and slows down the distribution system. Our method enhances decision-makers' ability to manage the resilience of supply chains.

INTRODUCTION

The complexity of supply chains—connecting manufacturers, distributors, retailers, and final buyers—has increased over the past century, raising concerns about their resilience (*1*–*5*). Recent events such as the COVID-19 pandemic, the war in Ukraine, and US-China trade disputes have affected supply chains by severely disrupting the global distribution of raw materials and goods. Following the COVID-19 pandemic, the US administration declared the "Public Health Supply Chain" a top national security issue and is seeking "new approaches to build diversity and flexibility" (*6*). To do so, policymakers and firms must quantify and devise policies to improve supply chain resilience, which is the ability to mitigate shortages following sudden reductions in products' availability.

There are several ways to tackle product shortages (*7*, *8*). However, there are two responses immediately available: rationing and substitution. While rationing may become necessary as the shortage deepens, substitution is the first choice as it affects final buyers the least. Mitigation strategies at the manufacturer level include raw material substitution, product redesign, or repackaging. At the distributor level, the focus of this work, these options are not available as distributors do not have manufacturing capabilities. Their only option is to search for substitutes elsewhere.

While much of the current research focuses on sourcing alternative products by establishing new supply relations (*9*, *10*), we argue that leveraging existing relations can also effectively mitigate shortages. Specifically, distributors can source substitute products from their direct suppliers and the suppliers of their suppliers, i.e., via existing relations. This strategy does not require the creation of new connections, which is costly and time-consuming (*11*). Moreover, it does not require specific action from the manufacturers, such as product or package redesign; hence, production dynamics are not considered.

Leveraging existing relations requires relaxing product preferences. This means that distributors and final buyers accept some substitute products from existing distributors. These substitute products then traverse the system via existing distribution paths but following pathways not yet used. Inspired by seminal works (*12*–*14*), we call this strategy reroute flexibility. We show that policies fostering reroute flexibility can considerably alleviate shortages, thus enhancing system resilience.

An ideal dataset to study the power of reroute flexibility in the pharmaceutical industry is the Automation of Reports and Consolidated Orders System (ARCOS) (*15*). It lists all drug shipments from 2006 to 2014 in the US opioid distribution system. A system that has often been affected by shortages with notable consequences (*16*–*20*). This dataset offers an unprecedented view of distribution at a systemic scale, which is unique in supply chain research (*21*). With these data, we reconstruct 40 billion distribution paths connecting manufacturers to more than a thousand distributors and 200,000 final buyers, i.e., pharmacies, hospitals, and practitioners. On the basis of the reconstructed paths, we develop and estimate a data-driven model to investigate (i) how supply shocks lead to shortages and (ii) how fostering reroute flexibility mitigates them.

RESULTS

Enhancing resilience through flexibility

Resilience is defined as a system's capacity to withstand, adapt, and recover from disruptions (*22*–*24*). There are three distinct ways to bolster the resilience of complex, interconnected systems (*25*, *26*). First, we can increase their robustness, i.e., their capacity to absorb disruptions (*27*–*29*). In the case of supply chains, this includes mandating higher safety stocks and supplier diversification (*16*). Second, we can increase the system's adaptive capacity (*30*, *31*), for example, its capacity to create new connections with backup suppliers and reroute products along existing pathways (*3*, *32*). The former may be costly and time-consuming, while the latter is immediately available (*11*). Such an adaptive capacity is usually referred to as flexibility (*33*–*35*). Third, we can increase the system's restorative capacity, i.e., its capacity to return to normal operation (*36*, *37*). Examples of restorative capacity are monetary capital, repair vehicles, and repair crews (*38*).

Previous studies (*39*, *40*) have shown that flexibility is crucial to adapt to drastic environmental disruptions, such as epidemics, political instability, wars, and natural disasters. They may affect a

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particular area of the system, e.g., a manufacturer, but then propagate through the whole system (*40*). These disruptions are typically low-probability but high-impact events with possible short- or long-term adverse effects.

Existing works (*9*, *41*–*43*) investigate flexibility as the capacity of a firm in creating relations with new suppliers in the aftermath of a disruption. However, this requires time and additional costs (*24*, *44*). Discussing a more rapid response (*32*, *45*), consider rerouting flexibility as a way to address congested nodes and links, i.e., scenarios where nodes or links have reduced capacities to handle products and thus these need to be rerouted to avoid congestions. In this work, we extend this idea by combining rerouting with product substitution, introducing a broader perspective on rerouting flexibility. By considering substitution as well, we allow for a larger number of alternative but already existing distribution routes that can be leveraged to mitigate the effect of disruptions. Moreover, differently from (*46*), we do not assume that all the paths linking manufacturers to final buyers have the same length. This assumption is a limitation as there is no fixed number of intermediary steps, especially in the distribution part of the supply chain. There are shortcuts, longer paths, and even loops (*47*–*49*).

Operationalizing reroute flexibility using upstream preferences

To operationalize reroute flexibility in a distribution system, we focus on the distributor of a good rather than the good itself. To understand this change of perspective, consider the example in Fig. 1. It shows a distribution system of two substitutable goods: green and blue. Distributor E prefers goods coming from A (green) over C (blue). We formalize these upstream preferences as stochastic chains with memory (*50*, *51*). These correspond to the probabilities that E places an order to D for goods coming from A or C. In this case, $\Pr(E \to D \to A) = 1$ and $\Pr(E \to D \to C) = 0$, respectively. However, if E had no specific preferences regarding A (green) or C (blue), then it would instead receive goods solely based on their availability in D. This implies that E would adapt to the preferences of its upstream distributor D. Thus, $\Pr(E \to D \to A) = \Pr(D \to A) = 0.5$ and $\Pr(E \to D \to C) = \Pr(D \to C) = 0.5$. Flexibility ϕ_E is the propensity of distributor E to relax its preferences in favor to those upstream. Formally

$$\begin{aligned}\Pr(E\to D\to A\,|\,\phi_E) &:= \phi_E \Pr(E\to D\to A) + (1-\phi_E)\Pr(D\to A)\\ \Pr(E\to D\to C\,|\,\phi_E) &:= \phi_E \Pr(E\to D\to C) + (1-\phi_E)\Pr(D\to C)\end{aligned} \quad (1)$$

When $\phi_E > 0$, distributor E becomes more flexible in its preferences and starts sourcing goods from C, thus opening up an alternative distribution path: $C \to D \to E$. Through this new path, E can fulfill its demand by substituting the good (green) it needs with the substitute (blue) coming from C. For instance, suppose E has a deficit of 4 green units, and D has a total stock of 4 units (2 green and 2 blue). If $\phi_E = 0$, then E would only be able to fulfill 2 units of its demand by receiving 2 green units. Instead, if E partially relaxes its upstream preferences ($\phi_E = 0.5$), then E could further reduce its deficit by an additional unit.

Note that reroute flexibility depends on the existence of upstream multisourcing—some distributors have at least two upstream distributors. Without multisourcing, there is a single path from any source to destination, leaving no alternative paths to leverage. Formally, this would imply that $\Pr(E \to D \to A) = \Pr(D \to A)$ and hence $\Pr(E \to D \to A|\phi_E) = \Pr(E \to D \to A)$ for all ϕ_E. The formalization of reroute flexibility requires a set of assumptions that we summarize in Table 1.

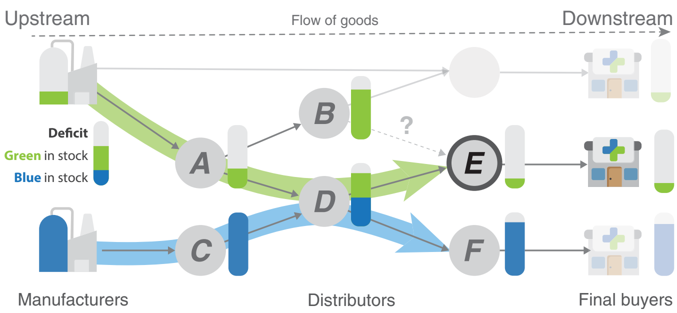

Fig. 1. Schematic illustration of a distribution system of two perfectly substitutable products: blue and green. Goods flow from upstream to downstream distributors and orders in the opposite direction. Gray arrows represent shipments of goods from one distributor to another. The two bold colored arrows are distribution paths, i.e., sequences of distributors through which goods arrive at their destination (final buyers). In this example, there is a shortage of green, shown by the deficit of green at both distributors and final buyers, while blue is fully available. Distributor *E* has demand for green, exceeding the stock available upstream at *D*. *D* could satisfy the demand with blue, a substitute. This is only possible if *E* relaxes its upstream preference for green and accepts blue instead. Alternatively, *E* could establish a new relation with *B* to obtain green (dashed line). Assuming that the cost of establishing a new relation is higher than substituting blue for green, *E* should choose the latter. This work focuses on this substitution, i.e., relaxing upstream preferences. The role of manufacturers is to hold inventory and distribute products to downstream distributors. No production dynamic is modeled.

Flexibility alleviates shortages

We analyze the distribution systems of the three most widely sold opioids in the United States: oxycodone, hydrocodone, and morphine. In the main text of this article, we report the results for the oxycodone distribution system in 2012. In the Supplementary Materials, we further repeat the analysis on multiple years and for the other distribution systems.

Stress test of distribution systems

We use stress test simulations to explore how empirical distribution systems may respond to supply shocks. Using a data-driven agent-based model, we simulate distributors placing orders based on demand and distributing goods based on orders. To simulate a sudden stop in production at $t = 0$, we reduce upstream distributor stocks by 70% of their maximal capacity inferred from data. We then analyze how this upstream deficit affects the final-buyers supply deficit and how the latter grows over time while production is halted. See the Supplementary Materials for a detailed explanation of the simulations.

Figure 2 shows the outcome of the stress test simulations on the oxycodone distribution system. These findings can be generalized to the other distribution systems as shown in the Supplementary Materials.

Figure 2A shows final-buyers supply deficit at different times. After 40 days, without flexibility, final buyers suffer a deficit of 6%. While this number might seem small, it corresponds to over 3 million missing oxycodone doses. This deficit continues to increase with time as the shortage remains unresolved and stocks are depleted.

Mitigating supply deficit

We consider how different levels of flexibility affect the final-buyer supply deficit, varying ϕ between 0 and 1. We assign the same flexibility ϕ to all distributors. It is worth noting that although each distributor shares the same ϕ, their individual influence on alternative path usage varies based on their respective positions in the disruption system and the volume of goods they handle.

As illustrated in Fig. 2A, introducing flexibility considerably reduces the deficit faced by final buyers. At $t = 40$, the deficit decreases from about 6 to 5% as ϕ increases from 0 to 1. This reduction means that about 500,000 more oxycodone doses are now reaching final buyers thanks to flexibility.

The largest reduction happens for some value ϕ^*, corresponding to the ϕ value yielding the lowest supply deficit. Notably, we find that ϕ^* may be smaller than 1 under specific stock allocations and distribution route conditions. For a more in-depth analysis of these conditions, along with insights into how individual distributors contribute to alternative path usage based on their positions and handled volumes, please refer to the Supplementary Materials.

Table 1. Summary of the operating assumptions for reroute flexibility. The role of these assumptions are discussed in Materials and Methods.

Operating assumptions	
Name	**Description**
Homogeneous products	Products are substitutable as long as they have the same active ingredient
Knowledge of substitutes	The existence of substitutes is known to final buyers and distributors
Fixed transportation time	Shipping between pairs of distributors takes a constant time
Low price elasticity	Prices do not affect demand and supply, hence, they are not modeled
No structural reconfiguration	Supply linkages do not change within a year
Long shelf life	Products do not expire on route
Equivalence of final buyers	Orders received by, e.g., hospitals have the same priority as the ones by pharmacies

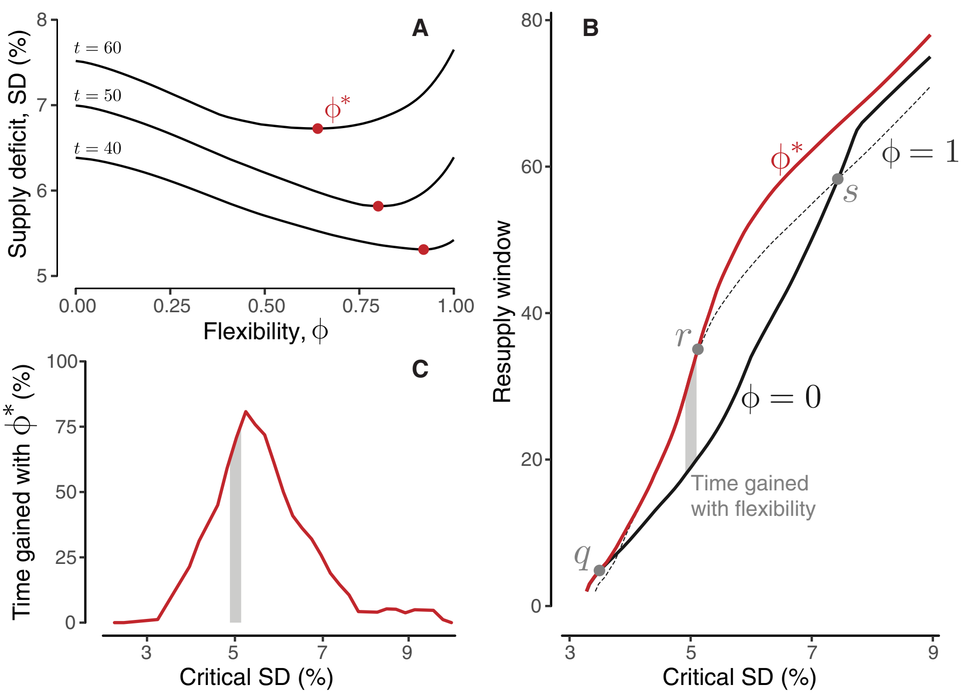

Fig. 2. Stress test simulation results for the oxycodone distribution system in 2012. (**A**) Percentage of final buyers' total demand that was not met, shown as the deficit, for reroute flexibility values $\phi \in [0,1]$. The results are plotted at 40, 50, and 60 days after production stopped. The reroute flexibility value ϕ^* yielding the maximum deficit reduction is shown in red. (**B**) Available resupply window shown as the time available to resupply before breaching a CSD, black line. The extended resupply window obtained with $\phi = \phi^*$, shown in red, is always above the black line. The resupply window obtained with full flexibility ($\phi = 1$) is shown as the dashed line. Up to point q, the resupply window is the same for $\phi = 0$ and ϕ^*. Beyond point r, the largest resupply window is obtained for $\phi^* < 1$. Beyond point s, full flexibility ($\phi = 1$) is worse than no flexibility ($\phi = 0$). (**C**) Time gained with flexibility, showing the increase in the time available for resupply for a given CSD.

Critical supply deficit

For essential goods, such as pharmaceuticals, a minimal supply level must be guaranteed. We use the term critical supply deficit (CSD) to refer to the maximum amount of goods that can be missing while still maintaining established standards. In the case of oxycodone, a CSD would be the maximum deficit that does not compromise patient safety. The concept of CSD is similar to that of service level agreements (SLAs), which set performance guarantees at the company level. However, CSD differs from SLAs in that it is a systemic measure considering all final buyers. In other words, the CSD indicates a critical deficit that system should not exceed.

Given an CSD, we define the resupply window as the latest possible time t at which resupply must happen before the deficit exceeds the CSD. We find that the resupply window can be considerably extended thanks to flexibility. In Fig. 2B, we show the maximum extension of the resupply window with flexibility for a given CSD. For small CSDs, the gain from flexibility is minimal. However, for larger values, the resupply window can be substantially extended. For example, if a supply deficit of 5% is critical, then the resupply must happen within 20 days without flexibility. With enough flexibility, the resupply window can be extended by up to 38 days.

In Fig. 2C, we show the percentage gain that can be obtained for different levels of CSD. We find that the resupply window can be extended by up to 80%. However, if the CSD is very low, e.g., 2%, then this CSD will be breached quickly. Thus, flexibility has no time to alleviate shortages. If the CSD is very high, e.g., 10%, when that supply deficit is reached, stocks will be depleted by regular demand. Hence, we identify a range of CSD where flexibility is particularly effective.

Empirical evidence for flexibility

Flexibility can mitigate supply deficits. Now, we provide evidence that distributors can indeed adapt their upstream preferences and thus increase their flexibility. We look at how empirical distribution systems evolve over time and assess the year-to-year flexibility $\widehat{\phi}_i(y)$ of each distributor. $\widehat{\phi}_i(y)$, defined in Eq. 7, captures how much distributor i relaxes its upstream preferences from year $y-1$ to year y. Precisely, we take a maximum likelihood approach to infer $\widehat{\phi}_i(y)$ given the upstream preference in year $y-1$ and the observed distribution paths in year y.

We find that, in every year, some degree of flexibility is present. While, on average, distributors' flexibility is low, large flexibility values are sporadically observed. To understand which distributors are more flexible, we compute the average position a distributor has on their distribution paths. For example, distributor D in Fig. 1 has position 2 in both the green and blue distribution paths. In Fig. 3A, we see how the average $\widehat{\phi}_i$ changes with positions. Distributors appearing at the beginning of paths have low flexibility, as do distributors at the end of paths, i.e., close to final buyers. Instead, distributors occupying middle positions are more flexible, with an average $\widehat{\phi}_i(t)$ as high as 0.25. A total of 95% of distributors occupying intermediate positions within the distribution system have a flexibility as high as 0.75. This suggests that (i) distributors are able to adapt their preferences and (ii) maximum flexibility depends on their position.

Balancing deficit reduction and the cost of flexibility

Flexibility introduces alternative distribution paths

We compute the proportion of goods distributed through alternative paths as flexibility increases. In Fig. 3B, we see that the usage of alternative paths grows monotonously with ϕ. In other words, the more flexible, the more likely are distributors to use alternative distribution paths. This allows final buyers to receive goods from multiple sources.

To understand where these alternative distribution paths are introduced, we visualize the distribution system in Fig. 3C. Blue edges show empirical distribution paths, while red edges represent the alternative paths available with full flexibility, i.e., $\phi = 1$. The zoom-in feature in Fig. 3C illustrates that introducing alternative paths (red) enables distribution between distributors who previously did not exchange goods, despite having a shared intermediary distributor. From Fig. 3C, we learn that the bulk of alternative distribution paths made available with flexibility is located toward the periphery of the distribution system.

The price of flexibility

In addition to increasing the usage of alternative paths, increasing flexibility may slow down or speed up distribution. On the one hand, flexibility may increase the usage of less direct paths, i.e., paths requiring more intermediate distributors before reaching final buyers, thus slowing down the distribution. An example of a less direct path is shown in the zoom-in feature in Fig. 3C. On the other hand, flexibility may also increase the usage of more direct paths, thus speeding up the distribution.

To estimate whether speedup or slowdown effects dominate, we compute the slowdown factor introduced in (*52*) and defined in Eq. 23. This factor indicates the proportion of additional distribution steps required to reach final buyers. By modeling the distribution of goods as a diffusion process, we estimate how the average distribution time scales with flexibility.

In Fig. 4A, we observe that increasing ϕ may both speed up and slowdown the distribution of oxycodone across the timeframe of our study. These results are confirmed when studying the distribution of other drugs, as reported in the Supplementary Materials. On average, however, there is a substantial slowdown that can exceed a factor of 2. Thus, as flexibility increases, goods tend to pass through more distributors, potentially raising handling costs. Additional costs may also arise, for example, because of labor and increased complexity. The observed slowdown and other additional costs indicate the existence of a trade-off between reducing deficit and using alternative paths.

Decreasing returns to flexibility

In Fig. 4B, we see the trade-off between deficit reduction and alternative path usage. The plot highlights the existence of an inefficient set located on the upper side of the curves (dashed line). For points in this set, a given deficit reduction is achievable at lower flexibility as well. In other words, the same deficit is attainable using fewer distribution paths and thus with lower costs. The set of points where this happens is the efficient set. Moreover, in Fig. 4B, we show that an efficient point at $t = 40$ becomes inefficient at $t = 60$. This occurs because the value of $\phi^*(t)$, separating the efficient from the inefficient set, decreases with time, which is also visible in Fig. 2.

DISCUSSION

Natural disasters, geopolitical tensions, and public health crises can severely disrupt supply chains, leading to shortages. Flexibility has been proposed as the crucial capacity of supply chains to adapt to these disruptions (*39*, *40*). Previous studies, however, have largely relied on theoretical models or small-scale case studies (*9*, *32*, *41*, *42*, *45*, *46*), leaving questions about the generalizability and real-world applicability of these findings.

Our investigation uses a data-driven approach to demonstrate that reroute flexibility—the ability to reroute and substitute goods via alternative distribution paths—can effectively mitigate supply deficits. Moreover, reroute flexibility can extend the time before a critical deficit is reached. To do so, we introduce a novel analytical tool for distribution systems based on stochastic chains with memory (*50*, *51*).

Reroute flexibility enables products to be distributed through existing yet underutilized distribution paths. These alternative distribution paths allow final buyers to receive either their preferred products or suitable substitutes. To identify these alternative paths, we introduce and formalize a path-based perspective tailored for

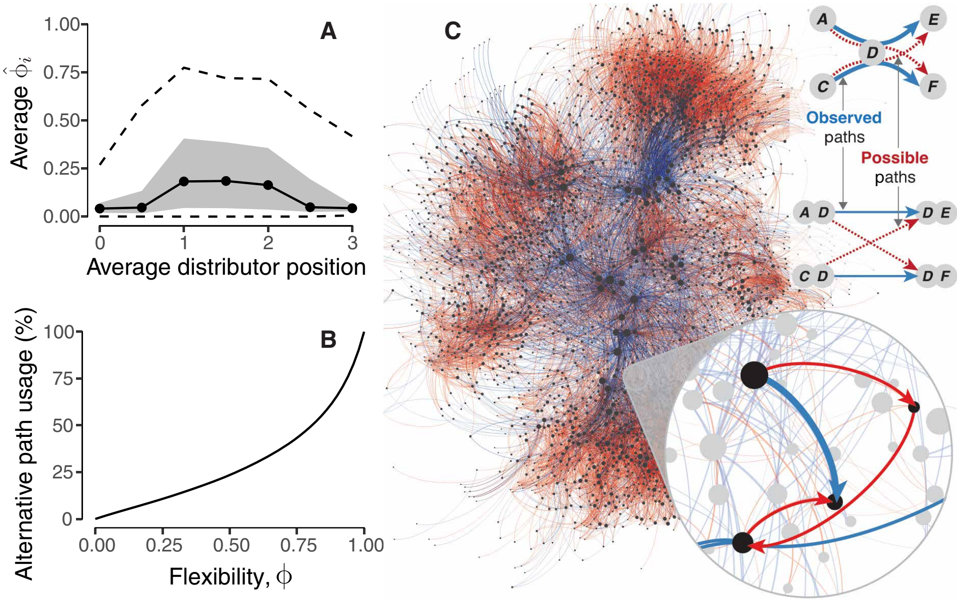

Fig. 3. Alternative distribution paths in the oxycodone distribution system. (**A**) Year-to-year flexibility ϕ_i of distributor *i* in the oxycodone distribution system from 2006 to 2014, shown as a function of the distributor's position on the distribution paths. The black lines represent the average flexibility, the shaded area shows the middle 50% of the data, and the dashed line shows 95%. (**B**) Proportion of goods shipped via alternative distribution paths 180 days after the stop in production, for different levels of flexibility ϕ. (**C**) The distribution system for oxycodone in 2012 represented as a second-order network. In this representation, a path of length 2, such as *A* → *D* → *E*, is depicted by an edge between the two "meta-nodes" (*A*, *D*) → (*D*, *E*) (as shown in the inset on the left). Blue edges indicate distribution paths that were observed, while the red edges represent alternative distribution paths that could exist. Increasing the parameter ϕ in this representation increases the probability that these red alternative paths become available for the distribution, in addition to the observed blue distribution paths. The zoom-in feature highlights that creating alternative distribution paths (red) allows previously disconnected nodes to connect. These alternative paths can be less direct than the observed blue paths, requiring products to follow longer routes.

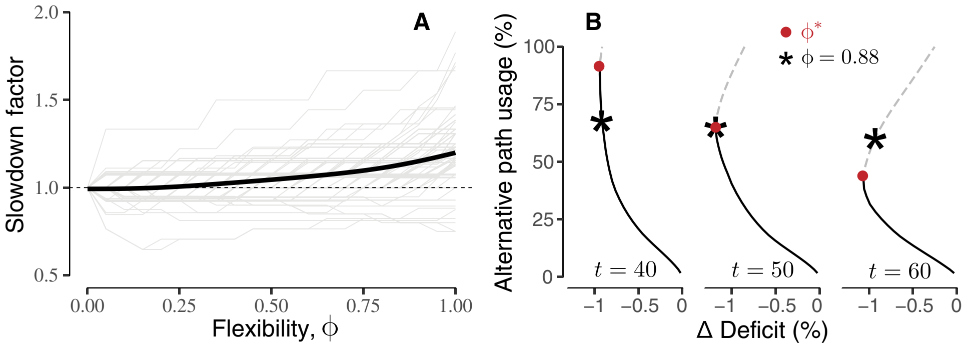

Fig. 4. The price of flexibility. (**A**) Slowdown factor for the oxycodone distribution system, as a function of ϕ. The solid line in the foreground indicates the average trend obtained from a standard generalized additive model smoother; the gray lines in the background show the different slowdowns obtained sliding a 1-year window from 2006 to 2015 by steps of 1 month. (**B**) Deficit reduction (Δ) versus alternative path usage, plotted at 40, 50, and 60 days after production stop. ϕ increases from bottom to top along the curves. Solid lines show efficient values of, while dashed lines show inefficient ones separated at $\phi^*(t)$. The point corresponding to $\phi^*(50)$ is shown in red, which is efficient at $t = 40$, has the highest deficit reduction at $t = 50$, and becomes inefficient at $t = 60$.

intertwined distribution networks, contributing to the existing supply chain literature.

Furthermore, our model enables us to assess the costs incurred when mitigating deficit via flexibility. Specifically, using alternative distribution paths may slow down distribution by requiring products to pass through additional intermediaries. These detours can increase both the handling costs and the complexity of the distribution network. Therefore, policy makers must weigh the potential benefits of increased flexibility against their costs.

Our findings are supported by existing research in the fields of supply chain management and operations research (*14*, *53*, *54*). Earlier studies have drawn attention to the tension between lean operations focusing on cost minimization and resilience-building strategies (*55*). Adopting resilience measures may introduce additional costs, including transportation, handling, and delays, that may clash with lean operational goals and adversely affect short-term financial performance (*53*, *56*). Therefore, these costs should be explicitly accounted for in risk assessments to enable a comprehensive evaluation of the trade-offs between increasing resilience and disruption-related costs (*57*).

While this study is based on a pharmaceutical distribution system, its implications are not limited to this sector. The inherent features that enable reroute flexibility—such as multisourcing—are commonly observed in many real-world distribution systems (*48*, *49*). Given the prevalence of these features across industries, our findings offer valuable insights not only for pharmaceuticals but also for other industrial sectors.

Limitations and future directions

Although the study offers important insights into the dynamics of distribution systems, it is important to note its limitations. This work relies on the ARCOS dataset, which tracks finished opioid products but does not provide details on individual firms or their operational strategies. Since more than 99.9% of all shipments occur between US firms and less than 0.1% are import/export transactions, the dataset gives a complete view of the US; however, it is US-centric. ARCOS does not include information on raw materials or other production inputs. This data limitation constrains the ability to investigate how these factors might influence the resilience of distribution systems.

Another limitation stems from the assumption of product homogeneity. Specifically, we adopt a nonrestrictive definition of product substitution, treating products with identical active ingredients as substitutable. This assumption does not account for final buyer preferences for specific packaging or dosages. Consequently, future studies could investigate the impact of more restrictive substitution criteria on reroute flexibility. Moreover, the model assumes products to have low price elasticity in the short term, which has been observed for pharmaceuticals (*58*). However, for products with high price elasticity, this assumption does not hold, and future research should expand on this.

Furthermore, the model assumes that both final buyers and distributors are aware of available substitutes. While this assumption holds if distributors promptly disseminate this information, resource constraints may limit the effective communication between stakeholders. This does not undermine the intrinsic value of reroute flexibility, but it does highlight challenges in its practical implementation. Last, note that environmental disruptions can affect not only production activities but also railroads, seaports, and logistics facilities. Future research could extend the scope to assess the effectiveness of reroute flexibility under these other disruption scenarios.

Bridging the gap between system and firm perspective

Our research adopts a systemic viewpoint, taking the entire distribution system as the unit of analysis. This approach is instrumental in monitoring systemic risk, such as shortages affecting all consumers. Drawing parallels with lessons learned from systemic risk in financial markets (*59*–*62*), we argue that systemic interventions are indispensable for dealing with disruptions in distribution systems. Expanding on the existing research in supply chain resilience and operations management, we explore reroute flexibility as a systemic intervention designed to mitigate such disruptions.

To effectively implement systemic interventions like reroute flexibility, continuous, real-time monitoring of the distribution system is paramount. Regulatory bodies can use monitoring and stress testing tools, like the one presented in this study, to quantify potential supply deficits and assess the need for intervention. If deficits exceed policy-determined CSD levels, regulators can take action, which may involve informing distributors about their potential losses and the systemic benefits of reroute flexibility. Access to granular, real-time data is vital for this process, and centralized track-and-trace databases, such as the European Medicines Verification System, offer an example. Combining regulation with real-time monitoring can effectively bridge the gap between localized disruptions and their global consequences.

Last, while this work focuses on systemic solutions, the responsibility for implementing reroute flexibility ultimately rests with individual firms. One avenue for enhancing flexibility involves firms forming alliances and entering into pre-agreements for route switching in emergency scenarios. Success in this strategy depends on investments in internal capabilities like coordination and redundancy (*14*, *40*). These are critical for ensuring effective communication, strengthening information systems, and preparing for labor or utility shortages.

Despite the high priority managers place on supply chain risks, investment levels remain suboptimal, possibly because the likelihood of disruptions and their systemic impact are underestimated (*63*). This underestimation arises from a tension between long-term planning and short-term profit objectives, as well as from the inherent challenges in estimating the likelihood of cascading disruptions propagating through the supply chain. Adopting an individual firm's perspective highlights that although rerouting flexibility is a reactive strategy, proactive actions—such as investing in company capabilities—are essential for its effectiveness.

Final remarks

Strengthening supply chain resilience, i.e., the ability to withstand and recover from shocks, was declared a top national security by US President Obama in 2012 (*64*). To reconstitute the flow of commerce after disruption requires proactive and reactive measures. The former strengthens the supply chain's ability to withstand shocks, while the latter allows the system to adapt and mitigate the effects of disruptions. Proactive measures involve taking preventive action before disruptions occur, aiming to avert shortages altogether. Examples of proactive measures include mandating higher safety stocks, investing in just-in-case capacity, and pursuing diversification. Reactive measure prioritize swift responses after a shortage emerges. While proactive measures may require substantial upfront investments and, crucially, time, reactive measures are immediately available.

Reroute flexibility, a reactive measure, leverages existing resources such as infrastructure, business relations, and goods, making them immediately available without requiring new connections. However, reroute flexibility is costly due to increased handling time and distribution complexity. Consequently, there is a trade-off between its benefits and costs.

To manage this trade-off, regulators and policymakers must continuously monitor distribution paths to gain insights into how flexibility can extend the time until a critical deficit is reached. Our work provides the necessary tools to evaluate reroute flexibility and stress test the system continuously. Our analysis has highlighted that the most effective flexibility level changes with time, and the impact of flexibility is highest during the initial phase of a shortage. This becomes important when devising policies to foster reroute flexibility. Our approach is applicable to a broad range of products, not just pharmaceuticals, and is well-suited for substitutable products with partially overlapping distribution systems, e.g., grain, gas, and oil. By carefully balancing policies that foster reroute flexibility and costs, supply chains can become more resilient, enabling them to adapt to disruptions.

MATERIALS AND METHODS

Data

The ARCOS dataset

To study the US opioid distribution system, we drawn on the ARCOS (*15*) dataset. ARCOS is a data collection system managed by the US Drug Enforcement Administration (DEA). It facilitates the reporting of shipping transactions of controlled substances by manufacturers and distributors. Using this system, the DEA keeps track of all controlled substance shipments from the point of manufacture to the dispenser. Since only the transactions involving opioid drugs are publicly available, our study specifically focuses on them.

These transactions include various information such as the sending and receiving entities, the quantity and good shipped, and the exact shipping day. Drugs are identified by their national drug code, which allows us to distinguish the labeler, active ingredient, product, and packaging forms such as 12-ml vials or 120 pill boxes. Most entities are classified as either manufacturers or distributors. In addition, there are pharmacies, hospitals, practitioners, analytical labs, and clinics (but not patients) that we refer to as "final buyers."

Substitutability and price elasticity

The extent to which substitution alleviates shortages depends on the substitutability of the products. The US Food and Drug Administration defines drugs to be "pharmacologically equivalent" if they contain (i) the same active ingredient, (ii) have the same dosage form, and (iii) are identical in strength and concentration. In this work, we follow this definition and consider product substitutable when the first requirement is met.

Another aspect affecting product substitutability is pricing. For example, if a substitute product would be more expensive, then its demand would be lower. Previous research (*58*), however, suggests that the consumption of medically necessary drugs, such as painkillers, is not significantly affected by short-term price increases. Furthermore, price increases do not stimulate supply, as noted by the US Food and Drug Administration in their report on drug shortages (*65*). This is primarily due to the low price elasticity of prescription drugs, which is caused by how necessary pharmaceuticals are reimbursed. Insurers and federal programs, rather than patients, are usually responsible for paying for these drugs. For these reasons, this study does not consider the prices of drugs.

From shipping transactions to distribution paths

We reconstruct the distribution paths of opioid drugs by tracking all ARCOS transactions in a time-respecting order. Specifically, we trace individual drug packages as they leave the manufacturing facility, pass through distributors, and arrive at final buyers, e.g., hospitals, pharmacies, or practitioners.

To do so, we monitor distributor stock levels and assume a first-in-first-out stock management policy: Older stocks are shipped out first. This policy minimizes the impact on the product's shelf life, which is crucial for perishable products such as medicine. The World Health Organization recommends in their "Good Distribution Practices" (*66*) that distributors follow a "first expiry/first-out" stock management policy.

Using the 500 million transactions in ARCOS for 2006–2014, we reconstruct 40 billion distribution paths of individual drug packages. The set of reconstructed paths is denoted as $P \coloneqq \{p_1, p_2, \cdots, p_S\}$, where each element of the set represents a distribution path. Specifically, a distribution path, $p_s = (k \to j \to \cdots \to i)$, denotes the sequence of distributors and manufacturers traversed by a single package on its journey from manufacturer to the final buyer. The path p_s starts with the manufacturer k, traverses the distributor j, and ends with the last distributor i that ships to the final buyers.

Model

From distribution paths to upstream preferences

The length of reconstructed paths varies between 1 and 4, and most of these paths have a length of 2. This means that, in most cases, the distribution process involves only one manufacturer and two subsequent distributors. Given this observation, we choose to model upstream preferences up to two steps upstream. We validate this modeling choice performing the model selection tests proposed by (*67*, *68*). The tests show that modeling the distribution system accounting for two steps upstream is statistically optimal, given the available data. Given that distribution path of length 2 are the most common and capture well the whole distribution system, we use them to define upstream preferences.

Let us consider the length 2 distribution path $p_s = (k \to j \to i)$, where k is a manufacturer and j and i are two distributors. Each length 2 path may appear as a full observation or as a subpath of a longer distribution path, i.e., $(\cdots \to k \to j \to i \to \cdots)$. We denote with $\widetilde{A}_{kji}$ the total number of occurrences of p_s in the data, summing all its occurrences as standalone path with those as subpath of longer distribution paths. Assuming perfect market clearing within the system (supply equals demand), the observed shipment amount corresponds to the orders placed. This means that $\widetilde{A}_{kji} = A_{ijk}$, where A_{ijk} indicates the amount of orders placed by i to k, via the intermediary j. Hence, from A, we construct the two-step tensor, $T^{\text{2-step}}$, as

$$T_{ijk}^{2-\text{step}} = \frac{A_{ijk}}{\sum_{j'k'} A_{ij'k'}} \tag{2}$$

whose entries represent stochastic chains with memory (*50*, *51*). Formally, each element of $T^{\text{2-step}}$ represents the transition probability of an order moving along a path, or chain, of length two. For example, the entry $T_{ijk}^{2-\text{step}}$ is the probability that i submits an order to k via the intermediary j, i.e., $\Pr(i \to j \to k)$. By this, we capture preferences up to two steps upstream.

Relaxing upstream preferences

Distributors may relax their upstream preferences and, in the most extreme case, accept goods independently of their origin. To capture this tendency, we introduce a one-step transition matrix, S, whose element S_{ij} captures the probability that i places an order to j, i.e., $\Pr(i \to j)$. Formally, we write $S_{ij} = \sum_k T_{ijk}^{2-\text{step}}$ where the sum runs over all k. Using this one-step transition matrix, we construct a new tensor, $T^{\text{1-step}}$, that captures preferences up to one step upstream while modeling paths of length 2

$$T_{ijk}^{1-\text{step}} = \frac{S_{jk}}{\sum_{k'} S_{jk'}} \cdot \Theta\left[\sum_{k'} A_{ijk'}\right] \quad (3)$$

where $\Theta[x]$ equals 0 for $x \leq 0$ and equals 1 otherwise. The Θ ensures that we only consider a distributor j if there is at least one order placed by i toward j, and hence, no new links are created. Also, note that, except for the Θ, the right-hand side of Eq. 3 has only two indices (j,k), while the left-hand side has three (i,j,k). This is not a mistake. We are assuming that i has fully relaxed its upstream preferences, aligning them to the intermediary j. Consequently, the orders placed by i toward k do not depend on i anymore, but they only depend on the orders placed by j toward k.

Flexibility

Upstream preferences are relaxed according to the level of the distributors' flexibility. To model different levels of flexibility, we combine the $T_{ijk}^{1-\text{step}}$ and the $T_{ijk}^{2-\text{step}}$ as

$$T[\phi_i]_{ijk} = (1-\phi_i) T_{ijk}^{2-\text{step}} + \phi_i T_{ijk}^{1-\text{step}} \quad (4)$$

where ϕ_i is a parameter used to interpolate between the two limit cases: (i) the case where upstream preferences are perfectly preserved, captured by $T^{\text{2-step}}$, and (ii) a fully flexible case, captured by $T^{\text{1-step}}$. Its value ranges from zero to one and indicates the percentage of goods received by distributors independently of their upstream preferences. When flexibility equals zero, $T[\phi_i = 0]$ reduces to the two-step tensor, i..e, $T^{\text{2-step}}$. When flexibility equals one, $T[\phi_i = 1]$ reduces to the one-step tensor, i.e., $T^{\text{1-step}}$.

Empirical flexibility

We use a maximum likelihood approach to estimate the empirical flexibility of distributors at a given time horizon h. Specifically, we estimate the upstream preferences for each distributor by computing the shipment transition tensor $B[b, \phi]$ over a period $[t - b, t]$, where b is the period over which the preferences are estimated and ϕ is an n-dimensional vector whose entries ϕ_i correspond the flexibility of distributor i.

Specifically, we obtain $B[b, \phi]$ as the row normalized transpose of the order transition tensor $T[\phi, b]$ defined in Eq. 4. The rationale behind this is that we define expected shipments to be equal to expected orders assuming each distributor has placed orders for the observed volume. Formally

$$B_{ijk}[b, \phi_k] := \frac{T_{kji}[B, \phi_k] \cdot \upsilon_k}{\sum_{k'j'} T_{k'j'i}[b, \phi_{k'}] \cdot \upsilon_{k'}} \quad (5)$$

where $T_{ijk}[b, \phi_k]$ is defined in Eq. 4 over the period $[t - b, t]$ and $\upsilon_k = \sum_{lm} A_{klm}$ is the total volume ordered by k. We then construct from the shipments observed in the period $[t, t + h]$ the shipment tensor $\tilde{A}[h]$. The entry $\tilde{A}_{ijk}[h]$ captures the number of shipments from i to k via j in the period $[t, t + h]$. Last, we compute the likelihood of the observed shipments given the estimated transition tensor $B[b, \boldsymbol{\phi}]$ parametrized by $\boldsymbol{\phi}$ as

$$\mathcal{L}[\phi] = \prod_{i,j,k} B_{ijk}[b, \phi_k]^{\tilde{A}_{ijk}[h]} \propto \log\mathcal{L}[\phi] = \sum_{i,j,k} \tilde{A}_{ijk}[h] \log B_{ijk}[b, \phi_k] \quad (6)$$

The most likely parameter to have generated the observed shipments corresponds to the flexibility vector $\hat{\boldsymbol{\phi}}$ for which the likelihood is maximal.

$$\hat{\boldsymbol{\phi}} = \underset{\phi}{\text{argmax}} \left[\log\mathcal{L}[\boldsymbol{\phi}]\right] \quad (7)$$

In Fig. 3A, we estimate upstream preferences over a year ($b = 1$ year) and then use the estimated transition matrix to predict the shipments over the next year ($h = 1$ year).

Stress test simulation

Supply shock

We simulate an external shock that reduce the empirical production by σ percentage, i.e.,

$$s_i[t = t^*] = (1-\sigma)\, s_i[t-1] \; \forall i \in \{m_1, m_1, \ldots, m_n\} \quad (8)$$

where σ is the size of the shock and s_i[t] denote the manufacturer's stock level (used to store its production), and t^* is the time the shock hits the system.

Modeling distribution dynamics.

When the shock hits the distribution system, it can respond to it with various levels of flexibility. To model how distribution dynamics change depending on the level of flexibility considered, we extend the ARIO (Adaptive Regional Input Output) model introduced by (*69*). In this extension, we propose to incorporate the distributors' upstream preferences. According to the ARIO principles, distributors place orders to (i) meet demand and (ii) avoid empty inventories by keeping them at a constant target level, s^T, or safety buffer, i.e.

$$o_{(i|j)}[t] = d_{(i|j)}[t-1] + \frac{1}{\tau}(s_{(i|j)}^T - s_{(i|j)}[t]) \quad (9)$$

where $o_{(i|j)}$ is the order placed by i toward j and $d_{(i|j)}$ is the demand i faces on the goods received from j. The demand $d_{(i|j)}$ takes into account two terms: orders received from (a) final buyers and (b) orders received from other distributors. The term (a) is captured by the vector $\mathbf{c}$, and the term (b) is captured by the order matrix **O**. Following the approach in (*69*), we model the two terms separately.

The parameter τ indicates how quickly distributor i wants to restore its inventories. To keep our model simple, we consider τ homogeneous across distributors and constant over time. In our study, we set it equal to one working week, i.e., $\tau = 5$ days.

$s_{(i|j)}$ represents the substock of i used to store goods received from j. Note that unlike the original version of the ARIO model, in the presented model, distributors hold stocks divided into substocks. A substock $s_{(i|j)}$ represents the part of the stock used by i to store goods coming from j. In this way, we keep track of the stage before the goods enter the warehouse. Substocks are updated according to the total ship-out and the total ship-in

$$s_{(i|j)}[t] = s_{(i|j)}[t-1] + W^{\text{in}}_{(i|j)}[t-1] - (W^{\text{out}}_{(i|j)}[t-1] + \omega_{(i|j)}[t-1]) \tag{10}$$

The second term on the right-hand side indicates the total amount of goods i received from j. The third term, i.e., the one in parentheses, indicates the amount of goods shipped by i given that it has received such goods from j. This total ship-out captures both the amount directed to final buyers, $\omega_{(i|j)}$, and the amount directed to other distributors, $W^{\text{out}}_{(i|j)}$. Once stocks are updated, distributors places orders while respecting their upstream preferences captured by the tensor T_{ijk} as

$$O_{ijk}[t] = o_{(i|j)}[t] T_{ijk}[\phi] \tag{11}$$

where $T[\phi]$ is defined in Eq. 4. Thus, in the case of zero flexibility, $\phi = 0$, upstream preferences are kept fix. In the case of medium flexibility, $\phi \neq 0$, upstream preferences are relaxed. Last, assuming that distributors want to meet demand as much as possible, the quantity shipped by a given distributor i is always determined as the maximum between the orders faced by i and its stock level.

Initialization with real-world data

In a stress test approach, we want to start with the closest representation of the real system and simulate its deviation given a possible supply shock. Building on this reasoning, we initialize the demand from final buyers and the stock levels of distributors with the empirical data. First, we assume that distributors meet demand perfectly within the observation year, y. On the basis of this assumption, we determine the constant daily demand faced by distributor i as

$$c_i = \frac{\omega_i[y]}{365} \tag{12}$$

where $\omega_i[y]$ indicates the amount i shipped to final buyers in the year y. Taking into account the proportion of goods received by i source partners, we obtain the demand faced by i and conditioned on j as

$$c_{(i|j)} = c_i \frac{W^{\text{in}}_{(i|j)}[y]}{\sum_{j'} W^{\text{in}}_{(i|j')}[y]} \tag{13}$$

where $W^{\text{in}}_{(i|j')}$ is the amount of goods i sources from its partner j'. Next, we determine the target stocks assuming that all distributors meet their planning within the observation year. Under this assumption, the target stocks are obtained as the empirical buffer observed at the end of the year, as

$$s^T_i = W^{\text{in}}_i[y] - (W^{\text{out}}_i[y] - \omega_i[y]) \tag{14}$$

where the first term on the right-hand side indicates the total ship-in of i in the year y; whereas the second term indicates the total ship-out of i in the year y. Taking into account the proportion of goods received by i from its source partners, we compute the target substock of i conditioned to distributor j as

$$S^T_{(i|j)} = S^T_i \frac{W^{\text{in}}_{(i|j)}[y]}{\sum_{j'} W^{\text{in}}_{(i|j')}[y]} \tag{15}$$

All stocks are initialized to their target values at the beginning of the simulation. Note that, in some cases, the ship-out is bigger than the ship-in. This suggests that (i) their inventories were not empty at the beginning of the given year, or (ii) they did not plan a target (safety) stock. For these distributors, we set a minimum buffer equal to one.

Quantifying the effect of flexibility

Supply deficit

We define the supply deficit, $\delta[t]$, at time t, as the percentage of the (cumulative) unfulfilled demand of final buyers, i.e.,

$$\delta[t] = \frac{\sum_{t'=0}^{t} \sum_i \omega_i[t'] - c_i}{t \times \sum_i c_i} \tag{16}$$

where i runs over all distributors shipping to final buyers. Our indicator is built assuming that goods ordered are shipped within the next working day.

Alternative path usage

To quantify the usage of alternative distribution paths, introduced by flexibility, we consider the amount shipped in two scenario: when flexibility is zero and when it is different from zero. The difference between those two quantities gives the difference in the amount of goods shipped between every distributor pair when upstream preferences are relaxed. We normalize such absolute difference with the maximum possible difference, occurring for $\phi = 1$, thus obtaining

$$\Gamma[t] = \frac{\sum_{ij} \left| W_{(i|j)}[\phi, t] - W_{(i|j)}[\phi = 0, t] \right|}{\sum_{ij} \left| W_{(i|j)}[\phi = 1, t] - W_{(i|j)}[\phi = 0, t] \right|} \tag{17}$$

Slowdown factor

To compare the distribution speed at the change of flexibility and strict upstream preferences, we use the slowdown factor introduced in (*52*). Let M denote a row-stochastic transition matrix describing an aperiodic, irreducible random walk. Let π be the stationary distribution of M and $\pi^{(t)}$ the visitation probability distribution at time t starting from an initial distribution $\pi^{(0)}$. π exists and is unique since M is aperiodic and irreducible. The total variation distance between π and $\pi^{(t)}$ can be written as

$$\delta[\pi^{(t)}, \pi] := \frac{1}{2} ||\pi - \pi^{(t)}||_1 \tag{18}$$

where $||.||_1$ denotes the L^1 norm. Further, we compute $\pi^{(t)}$ as

$$\pi^{(t)} = \pi^{(t-1)} \cdot M = (\pi^{(t-2)} \cdot M) \cdot M = \pi^{(0)} \cdot M^t \tag{19}$$

For a given ε, we can approximate the diffusion speed over M as the minimum time $t_\varepsilon[M]$ such that $\delta[\pi^{(t_\varepsilon[M])}, \pi] \leq \varepsilon$. In the special case where M is diagonalizable, it can been shown (*52*) that $t_\varepsilon[M]$ scales with

$$t_\varepsilon[M] \approx \frac{\log[\varepsilon]}{\log|\lambda_2[M]|} \quad (20)$$

where $\lambda_2[M]$ is the second leading eigenvalue of M. However, in the general case, t_ε needs to be computed directly.

Consider now the $B[b, \boldsymbol{\phi}]$ tensor defined in Eq. 5 and by setting the vector $\mathbf{v} = 1$. Its elements $B_{ijk}[b, \boldsymbol{\phi}]$ are the probabilities of a shipment from i to k via j as a function of flexibility $\boldsymbol{\phi}$. We can map the $B[b, \boldsymbol{\phi}]$ $n \times n \times n$ tensor representing two-step transitions to an equivalent $n^2 \times n^2$ second-order transition matrix $\tilde{B}[b, \boldsymbol{\phi}]$ as follows. A second-order node (i, j) denotes that i ships to j in the distribution system. If the shipment from i to j does not exists, then the second-order node (i, j) does not exist (*52*, *67*). In the other cases

$$\tilde{B}_{(i,j)(m,k)}[b, \boldsymbol{\phi}] = \begin{cases} B_{ijk}[b, \boldsymbol{\phi}] \text{ if } m = j \\ 0 \text{ otherwise} \end{cases} \quad (21)$$

Let Ω denote the set of final distributors, i.e., of distributors that ship goods downstream to final buyers (patients, hospital, and pharmacies). By connecting each final distributor ∈Ω to an end-node †, we can model the fact that distribution paths end at final distributors [see (*68*) for more details]

$$\tilde{B}_{(\omega,\dagger)(\dagger)}[\phi] > 0 \quad \text{if } \omega \in \Omega \quad (22)$$

where, with an abuse of notation, we denote with (†) the second-order representation of the end-node. Last, we set $\tilde{B}_{(\dagger)(\dagger)}[b, \boldsymbol{\phi}] = 1\ \forall\ \boldsymbol{\phi}$. By doing so, we ensure that the stochastic chain defined by $\tilde{B}[b, \boldsymbol{\phi}]$ is absorbing, irreducible, and aperiodic. Thus, $\tilde{B}[b, \boldsymbol{\phi}]$ has a unique stationary distribution $\pi = (0, \ldots, 0, 1)$, where the last element corresponds to the end-node (†) and all random walks converge to (†). Note that the stationary distribution π of $\tilde{B}[b, \boldsymbol{\phi}]$ is independent of the choice of ϕ.

Let $\pi^{(0)} = [1/(|Q| - 1), \ldots, 1/(|Q| - 1), 0]$ be the uniform distribution over all states Q in $\tilde{B}[b, \boldsymbol{\phi}]$ excluding the end-node †. We define the slowdown factor $\sigma(\boldsymbol{\phi})$ as the additional number of steps it takes for $\pi^{(0)}$ to converge to π based on $\tilde{B}[b, \boldsymbol{\phi}]$, compared to the reference case where $\boldsymbol{\phi} = 0$

$$\sigma[\boldsymbol{\phi}] := \frac{t_\varepsilon[\tilde{B}[b, \boldsymbol{\phi}]]}{t_\varepsilon[\tilde{B}[b, 0]]} \quad (23)$$

Supplementary Materials

This PDF file includes:
Supplementary Text
Figs. S1 to S5

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