Proceedings of the 2022 Winter Simulation Conference
B. Feng, G. Pedrielli, Y. Peng, S. Shashaani, E. Song, C.G. Corlu, L.H. Lee, E.P. Chew, T. Roeder, and P. Lendermann, eds.

SIMULATION OF IT DATA INTEGRATION TO OPTIMIZE AN ANTIBIOTICS SUPPLY CHAIN WITH SYSTEM DYNAMICS

Ines Julia Khadri

Department of Engineering Sciences
Uppsala University
Lägerhyddsvägen 1 Box 534,
752 21 Uppsala, SWEDEN

Joe Viana

Department of Accounting and Operations Management
BI Norwegian Business School
Nydalsveien 37, Oslo, 0484, NORWAY

ABSTRACT

Supply chain (SC) optimization is essential for a firm to cope with everchanging market conditions and disruptions. New technologies have allowed for more advanced supply chain optimization. This paper uses system dynamics (SD) simulation to model the effects of data integration technologies on an antibiotic (AB) SC operation. The study aims to improve the AB SC to benefit all relevant stakeholders including the patient population. We evaluate how IT integration technologies can improve communication across the SC to mitigate or reduce the impact of the of disruptions on AB users. The presented model is under development and is subject to structural and parametric changes as discussions continue with stakeholders about the system structure and what data can be used and disclosed. Despite extensive SC optimization literature there has been a growing call of an evidence base to support decision making relating to national medicine policies.

1 INTRODUCTION

Today, the pharmaceutical industry is facing great challenge to maintain the availability of certain antibiotics (ABs) across global markets which are experiencing supply shortages and disruptions due to the complexities related to the supply chain (SC), and demand related disruptions including but not limited to the Covid pandemic, and the behavior related to the use of ABs. The vulnerability of supply chains is illustrated by upstream issues, such as the wider availability of raw material suppliers, influencing production, and from downstream influencing management decision makers from a business profitability perspective, all governed by policy structures (National Academies of Sciences 2022). In addition, the rise of antimicrobial resistance (Spellberg 2014; Stone et al. 2018) among patients to AB has made market conditions critical to industry producers.

Antimicrobial resistance, humans' resistance to antimicrobial agents especially anti-bacterial to treat infections is growing (Quadri et al. 2015; Nurse-Findlay et al. 2017; Tängdén et al. 2018). The concern is the overuse of antibiotics, to treat for example trivial conditions, increases the likelihood they become ineffective for treating more serious conditions. Not only are ABs becoming less effective it has led to the emergence of "superbugs". These are strains of bacteria that have developed resistance to many different types of ABs. With the rise of antimicrobial resistance, it is challenging to create business models that generate adequate sales figures and limit the consumption of the drug at the same time (Spellberg 2014). Many ABs are older "generic" drugs, they are no longer patent protected, and the profit margins are much lower than patented medicines. Increasing antibiotics resistance in the human bodies are posing new threats to the availability of the active pharmaceutical ingredients (APIs), the active substance which produces a medicines therapeutic effect, as the existing APIs become ineffective to treat the bacterial infections. Due to a shortage of availability to particular medicines, doctors are forced to give less focused and efficient drugs, which can induce adverse effects and contribute to antibiotic resistance (Spellberg 2014).

The SC complexities associated with supply and demand side interactions coupled with wider interconnectivity with multiple wider human, manufacturing, logistics systems illustrate that medicine SC need to be examined by tools that are capable of analyzing such complex systems, one such tool is System Dynamics (SD) (Sterman 2000).

SD has been used to better understand real world behavior and to design and implement strategic policies for the purpose of improving the behavioral patterns of the system (Lertpattarapong 2002). SD analyzes nonlinear dynamic systems making it a powerful tool for studying the dynamics of SCs and policy designs to improve their operation. From a SD viewpoint, a SC consists of a structure interconnected concepts which create a system of feedback loops, which model users are able to explore to better understand why certain dynamic changes arise (Linnéusson et al. 2020). Feedback within a system provides information, often with a delay, to indicate how it is performing relative to desired state. Two types of feedback loops exist positive or negative. Positive feedback loops are self-reinforcing, identified with R or a "+" in casual loop diagrams (CLD), where an initial disturbance leads to further change, suggesting the presence of an unstable equilibrium. Negative feedback loops are self-correcting or balancing loops, identified with B or a "-", following a disturbance, the system seeks to return to an equilibrium situation, e.g., a home heating system with a thermostat. The accurate identification of internal interactive relationships between system elements is key in a feedback system (Sterman 2000). In SD the produced models tend to focus on a macro model where the entities are aggregated into a number of variables connected by flows (Gustafsson and Sternad 2007).

As a management tool, SD helps system owners and policy makers study how the underlying structure and the parameters of the system lead to behavioral patterns (Lertpattarapong 2002), some of which may appear counterintuitive. In a dynamic SC several parameters can be incorporated into an SD model to understand how these affect a certain subject or core issue. Discrete event simulation (DES) and agent based simulation (ABS) were considered to model an AB SC as they are both powerful modeling tools (Law 2014). DES models tend to focus on operational level problems representing processes in detail, e.g. following the production process of individual tablets or boxes of tablets, and the data requirements, and incorporating holistic effects caused by feedback may be more challenging (Sterman 2000; Law 2014). Due to scope of the project as determined through discussions with stakeholders and the research project it was deemed more appropriate to model at a strategic level in the first instance which may be more suitable in SD (Sterman 2000; Law 2014). ABS like DES tends to focus on an individual and the data requirements as a result can be greater (Silverman 2018). In ABS the behavior and interactions between agents, results in system wide behavior emerging from these interactions.

In this case, to optimize an AB SC, a study on AB shortage was conducted within a collaboration platform PLATINEA: (Platform for innovation of existing antibiotics) in Sweden. This platform consists of several stakeholders including representatives from industry, government, hospitals, and academia collaborating to find solutions to the ABs shortage problem. It has identified and defined several policy interventions which could be applied to the supply chain to mitigate shortages or reduce their impact. One policy intervention identified was to integrate data through a computer system, to achieve better coordination and transparency across the SC and to reduce shortage. We use SD to investigate how AB shortages may be reduced through the use data integration technologies. The technologies tested are sharing Point of Sale (POS) data and implementing an Electronic Data Interchange (EDI) connection between the supplier and the contract manufacturing organization (CMO). EDI is a technology used for buyer-seller cooperation to respond more rapidly to consumer demand (Vrbová et al. 2018). The technology establishes a link between the firms through a computer-to-computer electronic communication. POS data is used as a technology that measures how much of the product the customer is buying on a transactional level, then this data is sent back electronically into chosen categories of the firm (inventory, sales etc.) (Simon 2008). During interviews and meetings PLATINEA stakeholders, it was suggested that the sharing of POS data and the use of EDI could enable better secure communication to reduce bullwhip and other ripple effects across the SC.

The remainder of the paper is structured as follows. Section 2 provides a brief literature review of selected system dynamics used in supply chain literature. The SD model development and validation as well as the data used are presented in section 3. Initial scenario analysis and selected results are presented in section 4. We conclude the paper in section 5 with a discussion of the key theoretical, modeling, policy insights and suggestions for future research/work.

2 LITERATURE REVIEW

We acknowledge the much wider SC literature available, utilizing a variety of theoretical perspectives including mathematical and simulation modeling techniques and we recommend (Li and Chan 2013; Vieira et al. 2020; Liao and Widowati 2021; Mustafee et al. 2021).

Previous scholars have applied SD to SCs since the early 2000s (Lertpattarapong 2002; Wu et al. 2006; Rebs et al. 2019). Several SD models have been presented at the Winter Simulation Conference to demonstrate the efficacy of the approach applied to SC research including but not limited to (Orcun et al. 2006; Briano et al. 2010; Behdani 2012; Aslam and Ng 2015; Li et al. 2015; Tan et al. 2017). Orcun et al. (2006) illustrated how SD captured the behavior of production systems at high utilization. This is essential as pharmaceutical manufacturers seek to operate as efficiently as possible to maximize profits. An SD model of short life cycle products e.g. toys, or electronic devices to examined improvements to SC resilience to an example disruption at a single SC echelon consisting of three stages of production (raw materials, semi-finished products, and finished products) (Briano et al. 2010). Although not short life products AB SC resilience to disruptions is essential to maintain population health and to decrease the likelihood of AB resistance caused by needing to use substitute AB when the primary AB is unavailable.

The choice of modeling approach, SD or DES, and how that influences SC model design decisions is important to consider (Behdani 2012). To address limitations of specific modeling approaches, hybrid simulation approaches (Brailsford et al. 2019), combining DES (Law 2014), SD and ABS (Silverman 2018) for SC system analysis to capture the complexity of SC have been proposed (Umeda and Zhang 2010). Tan et al. (2017) constructed a hybrid simulation model of a multi echelon SCs where the wider system was represented using SD and the target firm was modeled as an ABM. A SC case consisting of three retailers, two manufacturers and one part supplier were presented and disruption management policies evaluated. Aslam and Ng (2015) combined SD and multi-objective optimization to investigate different manufacturing strategies for an industrial partner, to minimize the total system work in progress (WIP) and the total delivery delay. Hybrid approaches such as these are where we would like to develop our model in the future, but our first step is to produce an adequate working SD model to engage with stakeholders.

Closest to our current prototype model is Li et al. (2015) who used SD to analyze the impact of information sharing in a generalizable three echelon SC to mitigate risk. In this model three decision making rules were assessed 1) no information sharing, 2) partial information sharing, and 3) full information sharing. We utilize this generic approach, simplify it, and apply it to an AB medicine supply chain case. The scenarios we analyze focus on no information sharing and full information sharing.

Modeling and simulation research on pharmaceutical SCs tends to focus on one or two echelons, e.g., the supplier and the wholesaler, and fails to take a systems view of the supply chain (Settanni et al. 2017). The selected generic SD models presented focus on one or two echelons as does this paper, there are a few exceptions (Li et al. 2015; Tan et al. 2017), but it is not as widespread as it should be (Settanni et al. 2017). We plan to expand the model to incorporate the wider system through discussions with stakeholders. This paper adds to the system view literature of SC within pharmaceutical SCs. This paper as part of the wider PLATINEA project examines the systemic effects of disruptions and interventions to mitigate and respond to them. The paper illustrates in the first instance the effects of better transparency/communication between system actors on supply level measures (service levels). This is the first step of a wider modeling project with the goal of illustrating the approach to system owners to support decision making.

3 A SYSTEM DYNAMICS AB SUPPLY CHAIN MODEL

A four echelon AB SC SD model was created capturing the 1) the "customers", the hospitals who acquire the AB to meet the need of the patients that they serve, 2) a contract manufacturing organization (CMO), which is the firm that produces the AB to be used in hospitals from the API, 3) an API producer, that takes excipients, other non-active pharmaceutical substances, to combine with active substances to produce the API and 4) the API producers suppliers, those who provide the excipients and other components to the API producer required to produce the API. The customers and the API producer's suppliers are treated exogenously in this iteration of the model. A high-level, overview of the stock flow diagram, the quantitative SD model is provided in Figure 1.

Figure 1 is a simplification of the model and only the key relationships and mechanics will be described. A brief explanation of stock flow diagram is as follows. The boxes with solid borders and capitalized text are stocks, which are used to record the level of a variable/factor of interest over time, e.g., the amount of inventory, or the number of outstanding orders. These stocks are filled and drained via rates, which are the arrows entering and exiting a stock (with an "egg timer" in the middle of them), connecting stocks to other stocks or connecting them to cloud like symbols. The cloud like symbols if not connected to other model components via arrows are exogenous to the system representing inputs from outside or outputs to outside of the scope of the model. Those texts which are neither stocks nor rates are either auxiliary variables or variables. These variables are connected to rates and stocks to influence the flow of material and or information through the stock flow diagram and ultimately how the model behaves. For a more comprehensive explanation of stock flow model mechanics consult (Sterman 2000; Morecroft 2015).

The distributors place orders for antibiotics "customers order rate". These orders are added to the "Order Backlog" stock via the "order rate". The orders are also used by the CMO to forecast production requirements and to set desired levels of finished goods inventory (FGI), work in process (WIP) inventory and the relevant levels of raw materials (RM), see the "CMO Order Forecast" stock and the associated rate. The "CMO Order Forecast" influences the "CMO desired inventory levels", which incorporate several auxiliary variables and variables to represent the required dynamics. The customers' orders are satisfied by the "CMO FGI shipment rate", which is determined by the "CMO order fulfilment ratio" which is a ratio of the "CMO desired shipment rate" and the "CMO maximum shipment rate", e.g., as the CMO FGI shipment rate increases the "Order Backlog" decreases.

An equivalent process happens at the API producer level but the customer order rate in this instance, are orders placed by the CMO, see "CMO RM requirements" in Figure 1. The "CMO RM requirements" is the amount of API required by the CMO to meet its production targets. The orders from the CMO are added to the CMO Order Backlog stock and the process to satisfy the orders is the same as the CMO production process subject to different parameter settings, which influence the production rate due to process times and other delays. The key parameters are presented in section 3.2. A simplifying assumption at the API level in this iteration of the model is that its suppliers replace exactly the RM used to produce the API (API RM delivery rate = API RM usage rate).

The shaded areas in Figure 1 represent a) the parts of the model used in the scenario analysis, with the value of those variables highlighted in black with white text, being changed, and b) the parts of the model highlighted in grey indicated those where outputs are collected to evaluate the SC performance with respect to the scenarios that are presented and discussed in section 4.

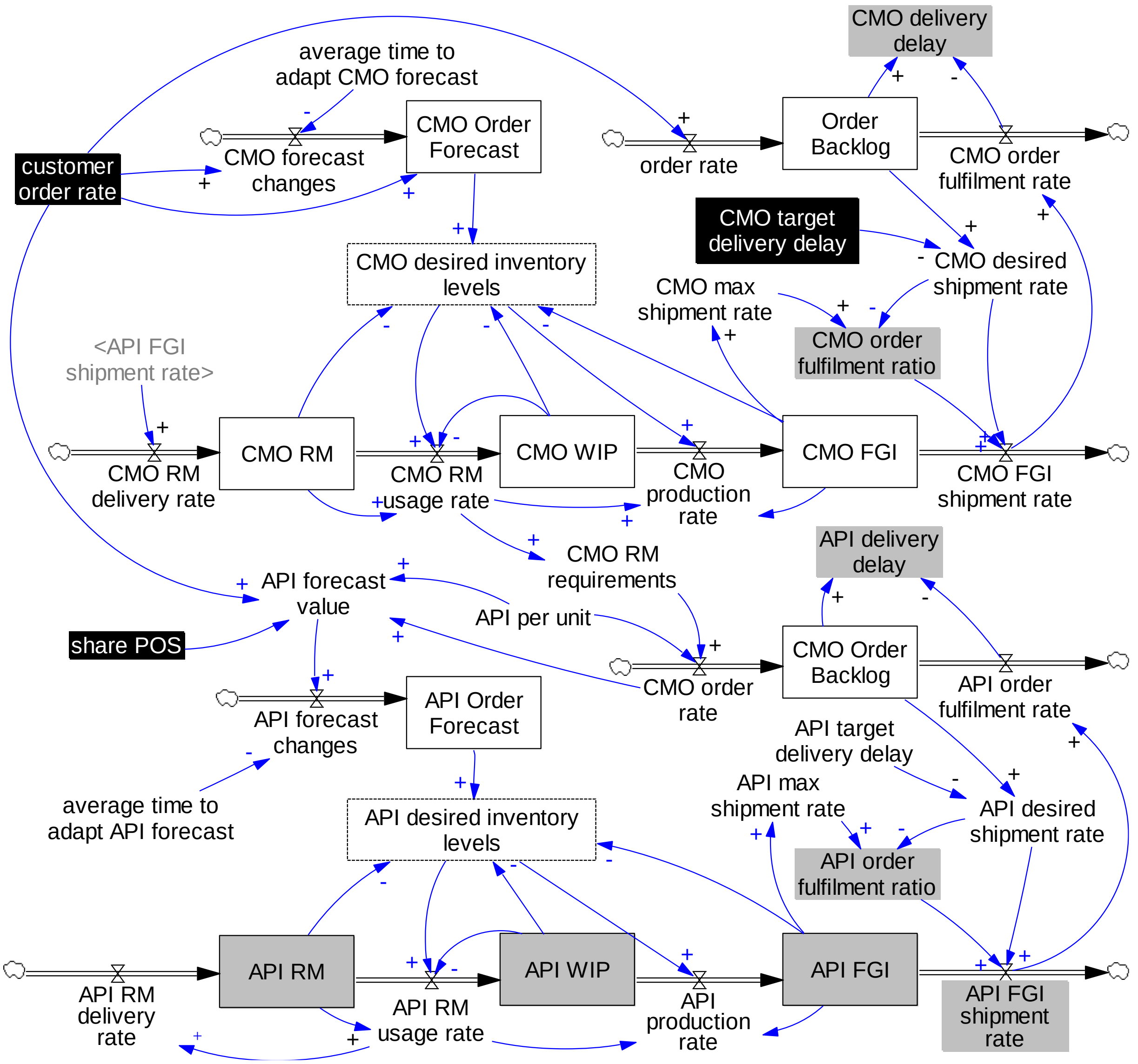

Figure 1: High-level model overview. Black variables indicate those used to test the scenarios analysis. Grey stocks and variables indicate presented outputs. Dashed variables denote visualization simplification.

3.1 Model Development

The model was built in VENSIM PLE 9.2.3. Due to the relative size and complexity of the model is split into multiple VENSIM views. The model and causal loop diagrams used to formulate the scope and boundaries of the model are available upon request. The dashed variables contain several auxiliary variables that link stocks and rates, including desired values and differences between actual and desired states to drive model behavior. Table 1 describes the key model rates. The model runs for 100 weeks in 0.125-time steps.

Due to the sensitive nature of medicine supply chains, in terms of regulatory and commercial requirements, the ongoing collection and negotiation of access to data, limited model validation has been performed. The validation tests performed include extreme value tests, face validated, including limited sensitivity analysis. Ongoing model development and validation will continue as better data become available, in terms of historical data and information about the behavior of the system from stakeholders.

Table 1: Model rates The RM usage rates refer to multiple variables and auxiliaries not presented for simplification purposes. DELAY3: Vensim function that returns a 3rd order exponential delay of the input

Name	Value/Equation
CMO forecast change	(customer order rate - CMO Order Forecast)/ average time to adapt CMO forecast
order rate	customer order rate
CMO order fulfilment rate	CMO FGI shipment rate
CMO FGI shipment rate	CMO desired shipment rate * CMO order fulfilment ratio
CMO production rate	DELAY3(CMO RM usage rate, CMO manufacturing cycle time)
CMO RM usage rate	Complex set of equations involving differences between desired and actual inventory levels triggering production and ordering, considering various variables (constraints). See table 2 for a list of the variables.
CMO RM delivery rate	API FGI shipment rate
API forecast change	((1-share POS) * CMO order rate + share POS * customer order rate * CMO material usage per unit) – API Order Forecast) / average time to adapt API forecast
CMO order rate	CMO RM requirements
API order fulfilment rate	API FGI shipment rate
API FGI shipment rate	API desired shipment rate * API order fulfilment ratio
API production rate	DELAY3(API RM usage rate, API manufacturing cycle time)
API RM usage rate	Complex set of equations involving differences between desired and actual inventory levels triggering production and ordering, considering various variables (constraints). See table 2 for a list of the variables.
API RM delivery rate	API RM usage rate (this is exogenous to the system and assumed in the first instance to be available).

3.2 Data Collection

Data have been collected from an anonymized antibiotic product from a CMO. Sales data for all antibiotics in Sweden, by packages and value (SEK) in Pharmacy, Hospital or mix was collected in months for the period 2013-2019. Due to limitations and restriction some data could not be collected therefore estimates provided by key stakeholders were used. The data provided by stakeholders and estimated and the model variables they relate to is presented in Table 2. Due to the structure of the model and that the CMO and the API stock flow diagram models share a similar structure, rather than add them as separate rows the “CMO” and “API” columns in Table 2 relate to the values of the respective variable for that organization.

The variables used in the model and their purposes are briefly summarized. The “customer order rate” is the average weekly orders received by the CMO from hospitals. The “share POS” is a binary variable indicating whether CMO forecasts can be shared with the API producer. The “step height” is used in a step function to increase the customer order rate by a given factor which happens at model time defined by “step time” in weeks. The “target delivery delay” is the desired time the CMO/API would like to deliver their products to their customers. The “average time to adapt forecast” is the time it takes the CMO/API to adjust their forecasts based on changes in ordering rates. The “inventory adjustment time” is the time the CMO/API need to adjust FGI to a desired level. The “(inventory) safety stock coverage” is the number of weeks demand of FGI the CMO/API would like to have in reserve. The “manufacturing cycle time”, is the average time it takes to transform WIP to FGI in the CMO/API. The “material inventory adjustment time” is the time the CMO/API need to adjust RM to a desired level, via ordering from the upstream SC echelon. The “material safety stock coverage” is the number of weeks demand of RM the CMO/API would like to have in reserve. The “material usage per unit” is the amount of RM required to produce a unit of FGI at the CMO/API. The “materials delivery delay perception time” is the delay in perceiving and responding to changes in supplier lead time at the API level. The “minimum material inventory coverage” is the minimum time required to prepare and utilize RM at the CMO/API. The “minimum order processing time” is the minimum time required to process and ship a customer order at the CMO/API. The "supply line adjustment time" is the average time to adjust the supply line to the desired level at the API level. The "WIP adjustment time" is the average time required to adjust the WIP inventory to the desired level at the CMO/API.

Table 2: Model variables. If equivalent CMO and API SFDs variables presented in the CMO and API columns, if not the value is present in the Value column. Source: E = estimate; S = Scenario; R = Real. Scenario values are indicated in brackets and the scenario number is indicated by the superscripted text.

Variable name	Value	CMO	API	Unit	Source
customer order rate	10,000			Widgets/week	E
share POS ^{S2}	0 (1)			Dimensionless	S
step height $^{S1, S2, S3}$	0 (0.2)			Dimensionless	S
step time $^{S1, S2, S3}$	5			Weeks	S
target delivery delay ^{S3}		2 (1)	2	Weeks	R/S
average time to adapt forecast		8	8	Weeks	E
inventory adjustment time		8	8	Weeks	E
(inventory) safety stock coverage		2	2	Weeks	E
manufacturing cycle time		8	8	Weeks	R
material inventory adjustment time		2	2	Weeks	E
material safety stock coverage		1	1	Weeks	E
material usage per unit		1	1	Material/Widget	E
materials delivery delay perception time			4	Weeks	E
minimum material inventory coverage		1	1	Weeks	E
minimum order processing time		2	2	Weeks	E
supply line adjustment time			2	Weeks	E
WIP adjustment time		2	2	Weeks	E

4 MODEL SCENARIOS AND RESULTS

In our scenario analysis, SC performance from the customer to the API producer, presented in Figure 1 is evaluated with these model outputs: 1) CMO order fulfilment ratio, 2) CMO delivery delay, 3) API FGI shipment rate, 4) API order fulfilment ratio, 5) API delivery delay, and the levels of the stocks 6) API FGI, 7) API WIP, and 8) API RM. The order fulfilment ratio = table for order fulfilment (maximum shipment rate / desired shipment rate), where table for order fulfilment is a function defining the non-linear relationship between shipment rate variables, which impact the shipment rates from the CMO and the API producer as, shipment rates = desired shipment rate x order fulfilment ratio. The Delivery delay = Backlog / Order fulfilment rate, is influenced by the order fulfilment ratio as, shipment rate = order fulfilment rate.

4.1 Model Scenarios

In the model we test a 20% step increase in customer orders (demand) after week 5 using a step function to increase weekly orders from 10,000 to 12,000 units per week. This scenario was chosen to investigate the effect on the CMO, and the API producer. Due to low profit margins and small demand for certain ABs, we assume that a competitor may exit the market increasing the demand for the CMO's product, which is a concern of public health agencies. The scenarios tested and potential interventions of sharing POS data (customer orders) between the CMO and the API producer for better production planning at the API producer (S2) and using EDI data to reduce the time it takes the CMO to satisfy customer orders (S3) are summarized in Table 3.

Table 3: Scenarios investigated. See Table 3 for scenario parameter values

Scenario	Description	Model change
Base (B)	Base case	None
Scenario 1 (S1)	20 % increase in demand	A competitor leaves the market
Scenario 2 (S2)	POS & 20 % increase in demand	Better forecasting at the API producer
Scenario 3 (S3)	EDI & 20 % increase in demand	Reduce CMO target delivery time

4.2 Model Results

In the base case the model starts in equilibrium, we assume static demand of 10,000 orders/week. Figure 2 presents the CMO's delivery delay for each scenario. Scenarios S1 and S2 exhibit similar behavior, with S2 taking slightly longer to recover due to reduced material delivery rate from the API producer because of POS data sharing. Implementing EDI (S2) reduces the CMO's target delivery delay from 2 to 1 week, this results in an expedited delivery. The delivery delay spikes at 2.10 (week 14.25), 2.10 (week 14.375), 1.07 (week 13.875) and returns to pre-disruption levels in weeks 28.125, 29.375, 27.625 for S1, S2, and S3 respectively. S3 has a higher percentage of increase in Delivery Delay relative to the pre-disruption Delivery Delay of 7.37 % compared to 5.11% for S1 and 5.13% for S2 but recovers to pre-disruption levels quicker.

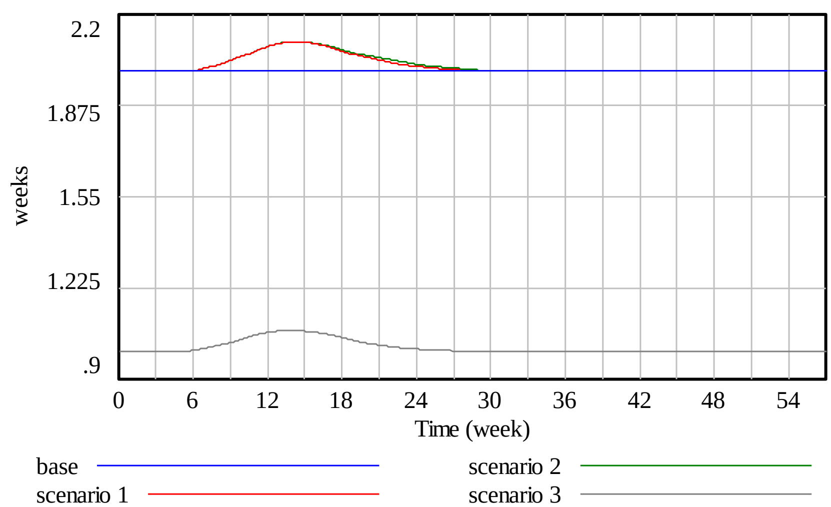

Figure 2: CMO's order delivery delay.

As the API producer's production planning process is based on forecasts of the CMO's customer order rate, this results in the clear bullwhip behavior exhibited for S1 and S3 in Figure 3. The bullwhip effect is stronger for S3 as the CMO is satisfying the customer's orders more rapidly which exacerbates the effect. The sharing of POS information between the CMO and the API Producer (S2) helps to lessen the bullwhip effect. The new shipment rate from week 5 is 12,000. It takes 85.625 weeks for S1 and S2 and 85.5 weeks for S3 to reach this value, note this is outside the presented time horizon. The maximum and minimum values for scenarios and the percentage above or below the required values are calculated. Note that the min values are calculated from week 12 onwards. For S1 the max of 19,319 (+61.00%) occurs at week 18.625 and the min of 6,528,12 (-45.60%) occurs at week 22.375. For S2 the max of 14,205 (+18.37%) occurs at week 29.75 and the min of 10,843 (-9.64%) occurs at week 35.75. For S3 the max 20,713 (+72.61%) occurs at week 18.625 and the min of 4,469 (-62.76%) occurs at week 23.125.

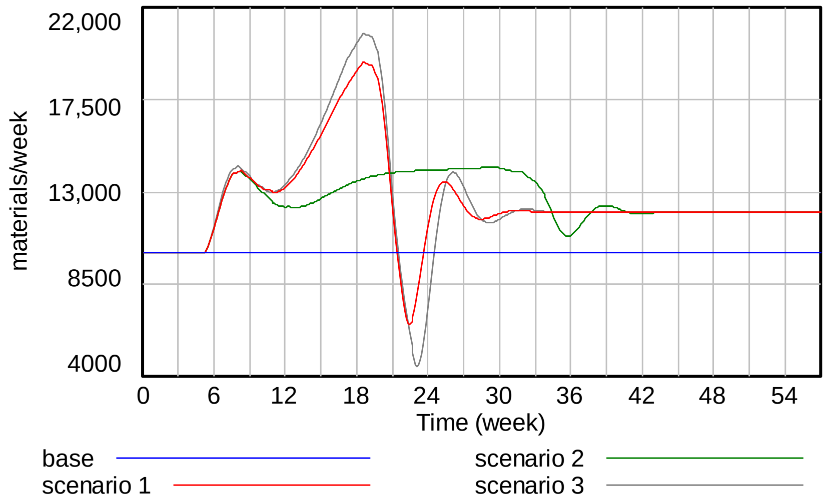

Figure 3: API FGI shipment rate.

The API producer's order fulfilment ratio falls to 37.79%, 16.64% and 32.53% for S1, S2, and S3 respectively. In addition to these drops the time order fulfilment ratio recovers to 100% in weeks 20.875, 39.875 and 20.875. Sharing of POS data (S2) results is detrimental order fulfilment ratio due to the increased delivery delay. The delay increases from 2 weeks to 5.29 weeks (164.59%), 12.02 weeks (500.85%) and 6.15 weeks (207.40%) for S1, S2, and S3 respectively. Figure 4 presents the API FGI inventory for each scenario, with the bullwhip behavior clearly evident in S1 and S3. The initial inventory following the disruption the drops for each scenario with lows of 26,657 (-44.46%), 24,477 (-49.01%) and 26,456 (-44.88%), for S1, S2, and S3 respectively. These lows occur at weeks 11.375, 12.875, 11.25. Unlike S2 which mitigates the bullwhip effect, resulting in a lower API order fulfilment ratio as production does not start to rise until week 34. The peak inventories were 79,562 (65.6%), 48,353 (0.7%), and 91,400 (90.4%) respectively. The highs occur at weeks 24.75, 48, 25.125. The scenarios approach the new equilibrium of 48,000 but there is continued fluctuation.

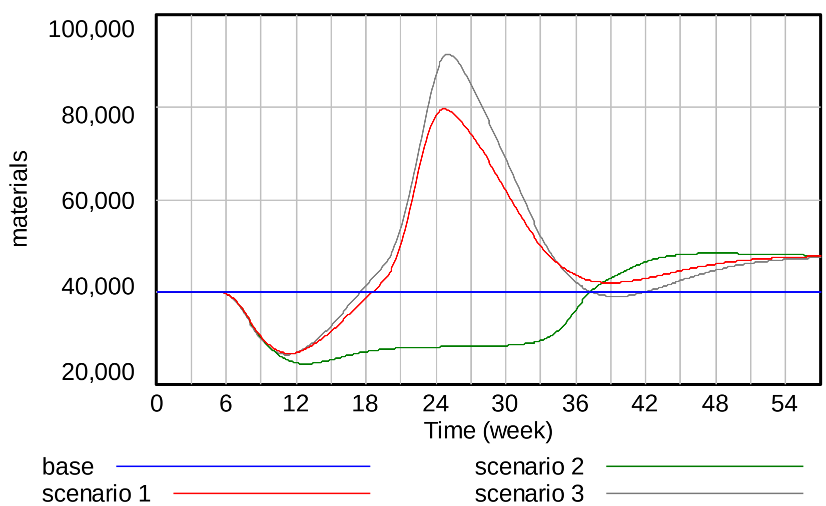

Figure 4: API FGI.

Due to the increased customer order rate and the drop in FGI, in S1 and S3 the amount API WIP increases rapidly as the forecasts do not include the POS data, presented in Figure 5. The peaks for API WIP are 182,138 (89.7%), 114,538 (19.3%), and 198,218 (106.5%) for S1, S2, and S3 respectively. These peaks occur in weeks 17.000, 31.125, and 16.625. The min values of 54,742 (-43.0%), 95,448 (-0.6%), and 41,869 (-56.4%) for S1, S2, and S3. These min values occur in weeks 25.875, 48.25, and 26.625.

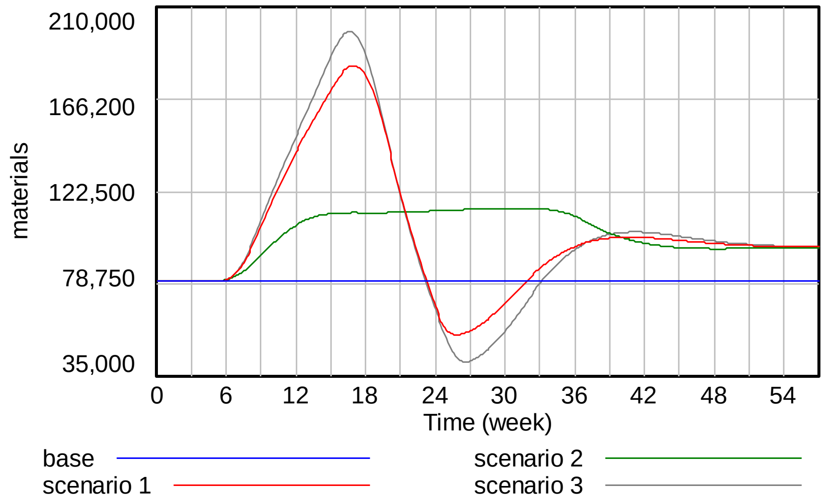

Figure 5: API WIP.

The API RM for each scenario is shown in Figure 6, with bullwhip behavior clearly evident in S1 and S3. The material inventory peaks at 51,793 (115.8%), 30,500 (27.1%), and 58,339 (143.1%) for S1, S2 and S3 respectively. These peaks occur in weeks 15.875, 11.75, and 15.625.

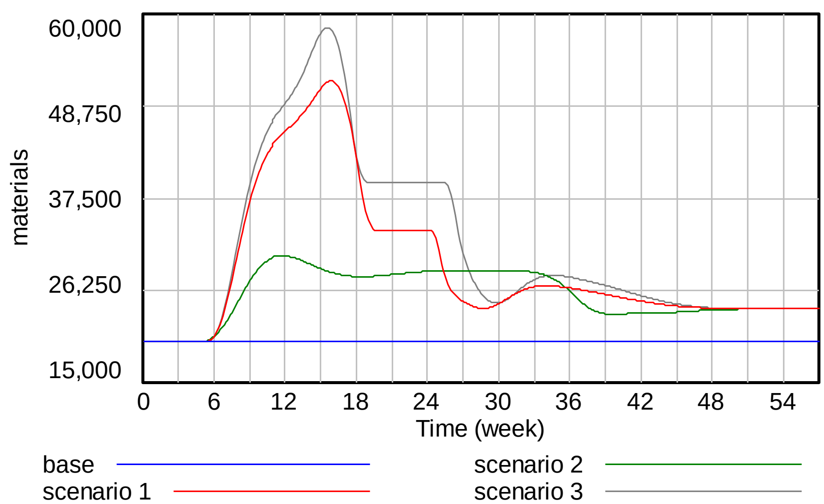

Figure 6: API RM.

5 DISCUSSION AND CONCLUSION

Our analysis suggests that when the supplier does not know final sales, they cannot determine between enduring or temporary change in consumer demand. The inventories at the suppliers are either excessive or insufficient to satisfy demand. However sharing POS data electronically with suppliers, eliminates delays and distortions in the information suppliers need to plan production and capacity lowering variance in inventories and material deliveries, resulting in a more stable SC, reducing the bullwhip effect (Croson and Donohue 2009). EDI yielded good results in the downstream, significantly improving firm's delivery delay, better serving the patient population, with however few downward effects on the upstream. Overall, this study showed that the two technologies helped in different ways improving visibility in the supply chain sharing POS provided better results in terms of stability whereas EDI reduced the firm's delivery delay.

The model makes several simplifying assumptions with respect to the structure of this complex system, the data used to parameterize the model, and the feedback mechanisms represented, which are continuously reviewed with the platform partners. PLATINEA has access to better quality data but due to non-disclosure agreements and other contractual obligations, we are not able to disseminate this information.

This paper assesses the effects of a demand disruption at a specific point in the AB SC. The PLATINEA project has identified several other interventions to respond to disruptions and to mitigate the effect of them. Simulation and mathematical modeling are valuable tools to quantify the effects of disruptions and interventions to manage or prevent them, and we anticipate that the current SD model could be expanded to look at several of these. Additionally, one could explore alternative modeling and simulation approaches such as DES (Doroudi et al. 2018) or hybrid modeling (Viana et al. 2021) to address specific problems.

ACKNOWLEDGMENTS

This work was supported by Vinnova. We would like to thank the organizations we've interviewed and the members of the PLATINEA team for their feedback and the constructive comments the reviewers.

REFERENCES

Aslam, T., and A. H. C. Ng. 2015. "Strategy Evaluation Using System Dynamics and Multi-Objective Optimization for an Internal Supply Chain". In *Proceedings of the 2015 Winter Simulation Conference*, edited by L. Yilmaz, W.K.V. Chan, I. Moon, T.M.K. Roeder, C. Macal, and M. D. Rossetti, 2033-2044. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Behdani, B. 2012. "Evaluation of Paradigms for Modeling Supply Chains as Complex Socio-Technical Systems". In *Proceedings of the 2012 Winter Simulation Conference*, edited by C. Laroque, J. Himmelspach, R. Pasupathy, O. Rose, and A. M. Uhrmacher, 1-15. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Brailsford, S. C., T. Eldabi, M. Kunc, N. Mustafee, and A. F. Osorio. 2019. "Hybrid Simulation Modelling in Operational Research: A State-of-the-Art Review". *European Journal of Operational Research* 278 (3):721-737.

Briano, E., C. Caballini, P. Giribone, and R. Revetria. 2010. "Using System Dynamics for Short Life Cycle Supply Chains Evaluation". In *Proceedings of the 2010 Winter Simulation Conference*, edited by B. Johansson, S. Jain, J. Montoya-Torres, J. Hugan, and E. Yücesan, 1820-1832. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Croson, R., and K. Donohue. 2009. "Impact of Pos Data Sharing on Supply Chain Management: An Experimental Study". *Production and Operations Management* 12 (1):1-11.

Doroudi, R., R. Azghandi, Z. Feric, O. Mohaddesi, Y. Sun, J. Griffin, O. Ergun, D. Kaeli, P. Sequeira, S. Marsella, and C. Harteveld. 2018. "An Integrated Simulation Framework for Examining Resiliency in Pharmaceutical Supply Chains Considering Human Behaviors". In *2018 Winter Simulation Conference (WSC)*, edited by 88-99.

Gustafsson, L., and M. Sternad. 2007. "Bringing Consistency to Simulation of Population Models--Poisson Simulation as a Bridge between Micro and Macro Simulation". *Math Biosci* 209 (2):361-385.

Law, A. M. 2014. *Simulation Modeling and Analysis*. 5th edition ed: McGraw-Hill Education

Lertpattarapong, C. 2002. "Applying System Dynamics Approach to the Supply Chain Management Problem". Massachusetts Institute of Technology.

Li, H., L. H. Lee, E. P. Chew, and Y. Long. 2015. "A Three-Echelon System Dynamics Model on Supply Chain Risk Mitigation through Information Sharing". In *Proceedings of the 2015 Winter Simulation Conference*, edited by L. Yilmaz, W.K.V. Chan, I. Moon, T.M.K. Roeder, C. Macal, and M. D. Rossetti, 2045-2056. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Li, J., and F. T. S. Chan. 2013. "An Agent-Based Model of Supply Chains with Dynamic Structures". *Applied Mathematical Modelling* 37 (7):5403-5413.

Liao, S.-H., and R. Widowati. 2021. "A Supply Chain Management Study: A Review of Theoretical Models from 2014 to 2019". *Operations and Supply Chain Management: An International Journal*:173-188.

Linnéusson, G., A. H. C. Ng, and T. Aslam. 2020. "A Hybrid Simulation-Based Optimization Framework Supporting Strategic Maintenance Development to Improve Production Performance". *European Journal of Operational Research* 281 (2):402-414.

Morecroft, J. D. W. 2015. *Strategic Modelling and Business Dynamics: A Feedback Systems Approach*. New York: New York: John Wiley & Sons, Incorporated

Mustafee, N., K. Katsaliaki, and S. J. E. Taylor. 2021. "Distributed Approaches to Supply Chain Simulation". *ACM Transactions on Modeling and Computer Simulation* 31 (4):1-31.

National Academies of Sciences, Engineering, and Medicine. 2022. *Building Resilience into the Nation's Medical Product Supply Chains*

Nurse-Findlay, S., M. M. Taylor, M. Savage, M. B. Mello, S. Saliyou, M. Lavayen, F. Seghers, M. L. Campbell, F. Birgirimana, L. Ouedraogo, M. Newman Owiredu, N. Kidula, and L. Pyne-Mercier. 2017. "Shortages of Benzathine Penicillin for Prevention of Mother-to-Child Transmission of Syphilis: An Evaluation from Multi-Country Surveys and Stakeholder Interviews". *PLoS Med* 14 (12):e1002473.

Orcun, S., R. Uzsoy, and K. Kempf. 2006. "Using System Dynamics Simulations to Compare Capacity Models for Production Planning". In *Proceedings of the 2006 Winter Simulation Conference*, edited by L. F. Perrone, F. P. Wieland, J. Liu, B. G. Lawson, D. M. Nicol, and R. M. Fujimoto, 1855-1862. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Quadri, F., M. Mazer-Amirshahi, E. R. Fox, K. L. Hawley, J. M. Pines, M. S. Zocchi, and L. May. 2015. "Antibacterial Drug Shortages from 2001 to 2013: Implications for Clinical Practice". *Clin Infect Dis* 60 (12):1737-1742.

Rebs, T., M. Brandenburg, and S. Seuring. 2019. "System Dynamics Modeling for Sustainable Supply Chain Management: A Literature Review and Systems Thinking Approach". *Journal of Cleaner Production* 208:1265-1280.

Settanni, E., T. S. Harrington, and J. S. Srai. 2017. "Pharmaceutical Supply Chain Models: A Synthesis from a Systems View of Operations Research". *Operations Research Perspectives* 4:74-95.

Silverman, E. 2018. "Methodological Investigations in Agent-Based Modelling : With Applications for the Social Sciences". In. Cham: Springer International Publishing : Imprint: Springer.

Simon, R. 2008. "The Abcs of Point of Sales (Pos) Data". *The Journal of Business Forecasting* 27 (4):5.

Spellberg, B. 2014. "The Future of Antibiotics". *Crit Care* 18 (3):228.

Sterman, J. D. 2000. *Business Dynamics : Systems Thinking and Modeling for a Complex World*. Boston: Irwin McGraw-Hill

Stone, M. R. L., M. S. Butler, W. Phetsang, M. A. Cooper, and M. A. T. Blaskovich. 2018. "Fluorescent Antibiotics: New Research Tools to Fight Antibiotic Resistance". *Trends Biotechnol* 36 (5):523-536.

Tan, W. J., W. Cai, and A. N. Zhang. 2017. "Integration Design of Supply Chain Hybrid Simulation". In *Proceedings of the 2017 Winter Simulation Conference*, edited by V.W.K. Chan, A.D'Ambrogio, G. Zacharewicz, N. Mustafee, G. Wainer, and E. H. Page, 493-504. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Tängdén, T., C. Pulcini, H. Aagaard, M. Balasegaram, G. L. Hara, D. Nathwani, M. Sharland, U. Theuretzbacher, and O. Cars. 2018. "Unavailability of Old Antibiotics Threatens Effective Treatment for Common Bacterial Infections". *The Lancet Infectious Diseases* 18 (3):242-244.

Umeda, S., and F. Zhang. 2010. "A Simulation Modeling Framework for Supply Chain System Analysis". In *Proceedings of the 2010 Winter Simulation Conference*, edited by B. Johansson, S. Jain, J. Montoya-Torres, J. Hugan, and E. Yücesan, 2011-2022. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers, Inc.

Viana, J., K. Van Oorschot, and C. Ardal. 2021. "Assessing Resilience of Medicine Supply Chain Networks to Disruptions: A Proposed Hybrid Simulation Modeling Framework". In Proceedings of *2021 Winter Simulation Conference (WSC)*, edited by 1-12.

Vieira, A. A. C., L. M. S. Dias, M. Y. Santos, G. A. B. Pereira, and J. A. Oliveira. 2020. "Supply Chain Data Integration: A Literature Review". *Journal of Industrial Information Integration* 19.

Vrbová, P., V. Cempírek, M. Stopková, and L. Bartuška. 2018. "Various Electronic Data Interchange (Edi) Usage Options and Possible Substitution". *Naše more* 65 (4):187-191.

Wu, J., C. C. Chen, and R. Tsai. 2006. "Using System Dynamics Approach to Construct a Performance Measurement Model for Pharmacy Supply Chain Management". *Journal of International Technology and Information Management* 15|:13.

AUTHOR BIOGRAPHIES

INES JULIA KHADRI is a PhD student at Uppsala University. Her work is focused into aupply chain networks of antibiotics, she is emedded in an empirical case of a collaborarion platform involving multiple global actors. ines.khadri@angstrom.uu.se

JOE VIANA is a Researcher on the MIA – Measures for Improved Availability of medicines and Vaccines research project, at BI Norwegian Business School, Oslo. He holds a Ph.D in Operational Research from University of Southampton, UK. His interests are the application of hybrid simulation to improve the operation of health systems. His email address is joe.viana@bi.no