Modeling a closed-loop vaccine supply chain with transshipments to minimize wastage and threats to the public: a system dynamics approach

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Abstract

Purpose – This study aims to focus on building a conceptual closed-loop vaccine supply chain (CLVSC) to decrease vaccine wastage and counterfeit/fake vaccines.

Design/methodology/approach – Through a focused literature review, the framework for the CLVSC is described, and the system dynamics (SD) research methodology is used to build a causal loop diagram (CLD) of the proposed model.

Findings – In the battle against COVID-19, waste management systems have become overwhelmed, which has created negative environmental and extremely hazardous societal impacts. A key contributing factor is unused vaccine doses, shown as a source for counterfeit/fake vaccines. The findings identify a CLVSC design and transshipment operations to decrease vaccine wastage and the potential for vaccine theft.

Research limitations/implications – This study contributes to establishing a pandemic-specific VSC structure. The proposed model informs the current COVID-19 pandemic as well as potential future pandemics.

Social implications – A large part of the negative impact of counterfeit/fake vaccines is on human well-being, and this can be avoided with proper CLVSC.

Originality/value – This study develops a novel overarching SD CLD by integrating the epidemic model of disease transmission, VSC and closed-loop structure. This study enhances the policymakers' understanding of the importance of vaccine waste collection, proper handling and threats to the public, which are born through illicit activities that rely on stolen vaccine doses.

Keywords Vaccine supply chains, System dynamics, Transshipment, Closed-loop supply chains, Sustainability

Paper type Research paper

Introduction

According to the World Health Organization (WHO) (for full list of abbreviations, see Appendix 1), approximately 510 million COVID-19 cases and 6.3 million deaths worldwide have been reported as of April 2022 [I]. Although there are different strategies for combating the COVID-19 pandemic, such as masking and social distancing (Kontogiannis, 2021), vaccination is the primary strategy to battle the coronavirus and decrease fatality rates (Liang *et al.*, 2021). Vaccinations are critical in curbing fatalities; however, the supply chain operations that allow vaccines to reach populations are complicated (Lee and Haidari, 2017).

The number of vaccines required to reach herd immunity changes as complex factors unfold; however, there have been efforts to estimate this quantity. For instance, Kwok *et al.* (2021) posit that conditions to achieve herd immunity depend on the country, ranging from about 15% to 77%, whereas Randolph and Barreiro (2020) provide an overall global estimate of 67%. Considering the need for at least two doses of the vaccination for each individual, and the world's population of about 7.8 billion, it can be estimated that approximately 16 billion vaccine doses are required. However, as Alam *et al.* (2021) stated, the vaccine manufacturers' collective capacity

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was about 10 billion total doses in May 2021. Therefore, there is a global vaccine shortage (Amankwah-Amoah, 2022).

Despite the vaccine shortage, the WHO reported back in 2005 that 50% of vaccines are wasted annually around the globe [II]. More recent estimates on this percentage are scarce. COVID-19 vaccine waste (i.e. expired vaccines and packaging) occurs due to immense purchase orders without estimating vaccine acceptance (intention to get vaccinated), inappropriate allocation models in vaccine supply chains (VSCs), storage requirements (low-temperature storage), low-capacity syringe design, incorrect dose administration and vaccination appointment no-shows (Klemeš *et al.*, 2021). The vaccine waste is deferred to be handled according to local regulations [III], which does not guarantee a central control or monitoring of waste handling. Moreover, vaccine waste has overwhelmed waste management operations (Klemeš *et al.*, 2020). The amount of vaccine waste coupled with the lack of proper monitoring creates the potential for mishandled vaccine waste, which has also been identified as a possibility for stolen vaccine vials [IV]. Some potential illicit activities have been identified by researchers regarding the COVID-19 vaccines, including but not limited to counterfeit/fake vaccines, substandard doses and vaccine theft (Farrell and Johnson, 2020; Bae *et al.*, 2020; Bolton, 2021).

In addition to illicit activities caused by vaccine waste, the proliferation of vials and syringe waste constitutes a significant threat to environmental sustainability (Guillot, 2021). According to Klemeš *et al.* (2021), approximately 85% of medical waste is non-hazardous waste, including vial and syringe discards. If collected, disinfected and stored appropriately, the vial and syringe waste is recyclable. However, recycling firms are hesitant to collect medical waste, and there may be strict regulations to handle outdated/expired vaccines (Klemeš *et al.*, 2021). Therefore, the firms should focus on supply chain redesign with a closed-loop structure so that VSC waste is handled and appropriately monitored. With only a closed-loop structure, the full extent of the potential vaccine waste reduction cannot be guaranteed, especially given the short shelf life of vaccines after thawing. In addition to the closed-loop infrastructure, a real-time vaccination monitoring system that plans, tracks and monitors vaccine delivery can be used to reduce information asymmetry and vaccine waste (Lejarza and Baldea, 2020; Mast *et al.*, 2021; Weintraub *et al.*, 2021; Fadaki *et al.*, 2022).

Currently, the Centers for Disease Control and Prevention (CDC) uses a vaccine tracking system (VTrckS) to place COVID-19 vaccine orders. VTrckS is an integrated web-based centralized vaccine tracking system that connects the public health sector and private partners to provide successful vaccine allocation, distribution, administration, monitoring, and reporting [V]. According to the CDC, some wastage is to be expected for any immunization campaign, and the number of unused vaccine doses (wastage) is tracked. However, the COVID Data Tracker does not yet provide this information [VI]. Furthermore, researchers posit that correspondence and coordination between different local and state levels are not always consistent, creating additional challenges for accurate real-time data (Lee and Haidari, 2017; Alam *et al.*, 2021). Moreover, accurately forecasting vaccine demand is quite challenging due to demand uncertainties. There is often trouble matching supply to demand in influenza VSCs (Lin *et al.*, 2021), which also applies to COVID-19 VSC (Alam *et al.*, 2021). Therefore, centralized IT systems must be kept up to date and used by all parties to improve forecasting.

During the COVID-19 pandemic, health-care providers opted for vendor managed inventory (VMI) systems to attain operational efficiencies due to the capability of VMI to apply just-in-time strategies (Patrinley *et al.*, 2020). For instance, VMI systems are used to minimize medical waste in hospitals (Weraikat *et al.*, 2019). The real-time capabilities built to support the VMI systems help uphold the closed-loop nature of the system due to its closer monitoring potential. A transshipment strategy with a VMI system can be used to manage vaccine inventories and reduce wastage (Fadaki *et al.*, 2022).

Transshipment, defined as the movement of goods within the same echelon, can provide benefits such as cost reductions (Herer *et al.*, 2006; Çömez-Dolgan and Fescioglu-Unver, 2015), customer service level improvements due to the balancing of inventory levels (Çömez-Dolgan and Fescioglu-Unver, 2015; Yan and Liu, 2018) and quicker delivery (Çömez-Dolgan and Fescioglu-Unver, 2015). Especially due to the latter two benefits, transshipments would be more than beneficial to use in the VSC (Rudi *et al.*, 2001). Given the remaining shelf life of vaccines, transshipments can allow quick shifts in inventory from areas with excess inventory to regions lacking inventory via the central inventory management system (Fadaki *et al.*, 2022). One of the main challenges with transshipments is the complexity of optimizing transshipment decisions due to the vast number of variables required (Robinson, 1990; Çömez-Dolgan and Fescioglu-Unver, 2015). Moreover, Çömez-Dolgan and Fescioglu-Unver (2015) identify lack of participation as another transshipment challenge in decentralized systems. However, centralized systems with enforced decision-making rules can help mitigate the lack of involvement.

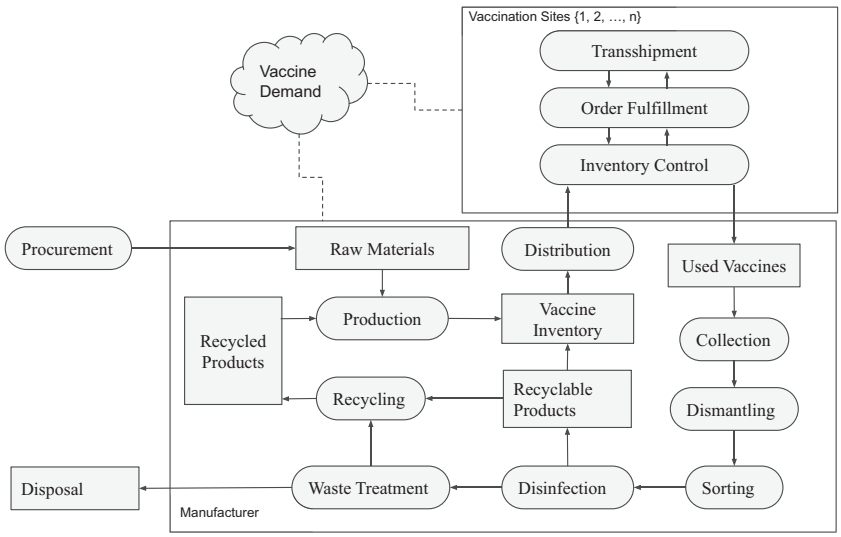
The WHO posits that access to genuine and good-quality vaccine doses should be uninterrupted for immunizations to work in VSC. The decoupled and often localized management of medication and vaccine providers challenges this objective. As the WHO asserts in their vision for a "successful immunization program," the goal is to:

> Strengthen supply chains to ensure that high-quality vaccines are always available in the right quantity and form at the right time, in the right place, and stored and distributed under the right conditions. Promote integration with other supply chains for more effective delivery of primary health care. Invest in systems and infrastructure to safely manage, treat and dispose of vaccine waste to help reduce their environmental footprint.

This vision calls for implementing impeccable logistics strategies along with collaboration among otherwise decoupled VSCs and suggests the need to consider the sustainability of operations via reducing the environmental footprint. While WHO's vision is well-intended, there is a need to take this vision one step further to build a sustainable VSC by integrating social impact considerations into strategies and operations. This integration is specifically proposed here since the threats of negative impacts that exist are not only environmental (Klemeš *et al.*, 2020) but also societal, such as theft and counterfeiting of vaccines (Bae *et al.*, 2020; Bolton, 2021; Amankwah-Amoah, 2022) and human well-being (Alam *et al.*, 2021).

In light of these considerations, this study aims to offer an overarching VSC model that can withstand the challenges of the pandemic by integrating transshipment operations and a closed-loop structure by using system dynamics (SD). The proposed VSC includes supplier, manufacturer/distributor and

Figure 1 Structure of the CLVSC with transshipment



vaccination site echelons. Figure 1 shows the proposed structure of the closed-loop vaccine supply chain (CLVSC) with the transshipment model.

The remainder of the paper is structured as follows. We first review the literature for SD. Next we build causal loop diagrams (CLDs) to propose our overarching SD model. Finally, we provide discussions and conclusions.

Literature review

Supply chains are complex systems that include information and materials flow within and outside supply chain partners; therefore, a systemic view helps explain supply chain complexity. General systems theory (Von Bertalanffy, 1950, 1968) suggests that different parts of complex operations should be evaluated and viewed as a whole. A system has a dynamic nature that allows interactions with sub-systems across boundaries (Caddy and Helou, 2007).

SD (Forrester, 1958, 1961) describes the structure of dynamic interactions among informational flows, physical processes and organizational policies and explains how these interactions improve system performance over time (Sterman, 2000). Lane (1999) defines SD as a structural theory of dynamic systems that includes accumulation processes, feedback loops and delays between cause and effect. "The development of SD models is a process in which modeling and empirical work take turns, providing a deductive-inductive balance" (Größler *et al.*, 2008).

System dynamics approach in health-care context

The SD approach has gained popularity over the years as one of the most effective approaches to analyzing and managing complex health-care challenges such as the occurrence of significant infectious or noninfectious diseases and the quality of health-care delivery (Homer and Hirsch, 2006; Samuel *et al.*, 2013; Darabi and Hosseinichimeh, 2020). In the vaccine context, Lee *et al.* (2017) investigate vaccine decision-making using the SD approach. Van Ackere and Schulz (2020) use the SD approach to examine vaccination decisions for measles. The majority of the health-care studies use the SD approach to model diseases, emergency care and delivery systems and health-care policies (Samuel *et al.*, 2010; Kumar and Kumar, 2014). Even though many SD studies contribute to the management and organizational science literature, few focus on managerial issues of health-care delivery (Darabi and Hosseinichimeh, 2020).

After the COVID-19 pandemic, the health-care SD studies' focus turned toward modeling the effects of pandemic mitigation strategies using metrics such as accessibility of medical sources, infection rate and contact rate (Kontogiannis, 2021). According to Kontogiannis (2021), these quantitative SD models do not address the complexity of the social and economic environment's influence on the spread of the disease. Therefore, Kontogiannis (2021) incorporates additional qualitative SD models built from system archetypes and integrates all the archetypes into an overall CLD to explain health-care challenges from a resilience perspective that includes anticipation of threats, resource provision, responses to uncertainties and process assessment within a resilience framework. In this study, we adapt Kontogiannis's (2021) methodology, develop multiple CLDs from an extensive review of the SD literature and combine them into an overarching model. The variables in CLDs are adapted from the models that were validated in previous studies in the literature (Vlachos *et al.*, 2007; Paul and Venkateswaran, 2017; Gonul Kochan *et al.*, 2018).

System dynamics in health-care supply chains

In the supply chain literature, Forrester (1958, 1961) developed the first supply chain SD model to evaluate inventory policies in a three-echelon supply chain. Since then, supply chain SD models have increasingly gained attention. These models are mainly used to analyze systems operations that change over time under various managerial policies (Sterman, 2000) and, more specifically, capture the production–inventory order behavior at an aggregate level using feedback-based structures (Venkateswaran and Son, 2007). Most supply chain studies use the SD approach to investigate the effects of coordination mechanisms such as VMI; collaborative planning (CP), forecasting and

replenishment (CPFR); and electronic supply chain management systems (e-SCMs) such as inter-organizational information technology (IT) integration, electronic data interchange (EDI) and cloud computing (Disney and Towill, 2003; Ovalle and Marquez, 2003; Machuca and Barajas, 2004; Fiala, 2005; Agarwal *et al.*, 2006; Wilson, 2007; Gonul Kochan *et al.*, 2018). These studies suggest that when IT is used effectively for coordination and information sharing, supply chain performance metrics such as service levels, inventory levels, costs and the bullwhip effect demonstrate improvement. More importantly, they find that SD modeling is appropriate for examining and understanding the information sharing in the supply chain structure.

In the health-care supply chain literature, only a few studies use the SD modeling approach to capture inter-organizational interactions (Gonul Kochan *et al.*, 2018). The contexts of these studies are waste management in health-care supply chains (Chaerul *et al.*, 2008), health-care service supply chain (Samuel *et al.*, 2013), inventory management and distribution of drugs (Azzi *et al.*, 2013), rural health-care supply chains (Kumar and Kumar, 2014), pharmaceutical supply chains (Asamoah *et al.*, 2011; Behzad *et al.*, 2011; Bam *et al.*, 2017), hospital supply chains (Gonul Kochan *et al.*, 2018) and vaccine supply chain (Kussainov, 2015). Specifically, Paul and Venkateswaran (2017) examine the effect of drug shortages of antiviral treatable disease epidemics on an infectivity/transmissibility parameter using an integrated SD model. The study uses a generic disease diffusion model that generates the supply chain demand and integrates the disease diffusion model (SEITRS) into a generic multi-echelon supply chain model. The combined model studies different supply chain factors such as delays, the number of echelons and ordering policies on the epidemic dynamics. Their findings suggest that these supply chain factors have a significant impact on epidemic dynamics. However, their model does not consider the perishability issues and capacity constraints. In this study, we develop a model that includes perishability and capacity constraints by closing the loop.

System dynamics in closed-loop supply chains

In sustainable SCM (SSCM) literature, SD modeling is lacking compared to analytical modeling and mathematical programming (Govindan *et al.*, 2015). Even though SD models are scarce in SSCM literature, these models help examine complex dynamic systems, identify causal links and mechanisms of environmental issues and facilitate long-term decision-making (Rebs *et al.*, 2019). Numerous studies examine inter-organizational interactions in closed-loop supply chains by using an SD approach. For instance, Vlachos *et al.* (2007) developed an SD model to examine the long-term behavior of closed-loop supply chains with remanufacturing and suggest efficient remanufacturing and capacity planning policies. Their generalized SD model combines a multi-echelon forward supply chain (producer and distributor) and reverse supply chain (remanufacturer and collector) that captures inter-organizational interactions. Later, Georgiadis and Besiou (2008) investigate the effects of ecological motivation and technological innovation on the long-term behavior of the closed-loop electrical and electronic equipment (EEE) supply chain. They introduce a novel closed-loop supply chain SD model comprising a forward supply chain with two echelons (producer and distributor) and a reverse channel encompassing recycling activities. Next, Georgiadis and Besiou (2010) extend their multi-tier closed-loop Waste EEE supply chain SD model to include environmental legislation effects. However, these aforementioned studies involve two echelons, mainly manufacturers and distributors. Our model contributes to the existing closed-loop SD literature by capturing the supply chain as a whole, including an additional echelon: retail (vaccination site).

According to Rebs *et al.* (2019), existing studies on closed-loop SD mainly focus on agriculture, automotive, biofuel, construction, electrical/electronics, energy supply, forestry/lumber, metal/mining, transportation and water supply industries. To the best of our knowledge, closed-loop supply chain SD modeling in the health-care industry has not been addressed in the literature.

There are many quantitative SD models at the micro-level that address health-care issues, mitigation strategies amid the COVID-19 pandemic, transactions and deliveries in health-care supply chains, policies and environmental issues in closed-loop supply chains. What is missing from the literature is an overarching SD model that addresses the issues in health-care supply chains, especially in VSCs, after the COVID-19 pandemic.

In summary, the major contributions of this study to the literature are as follows:

- extension of the SIR epidemic model for the COVID-19 pandemic;
- development of conceptual SD CLDs for vaccine transshipment operations;
- addressing the problems regarding the reverse flow of the COVID-19 VSC using CLDs; and
- development of an overarching CLD model to address the underlying structure of VSC, reverse VSC and transshipment operations and their connections and interactions to help organizations better navigate and distribute vaccines during future pandemics.

Methodology

As the first step of the SD modeling process, we first define the problem that encompasses the objective of this study and determine the system boundaries. Next, we identify variables and their interactions by reviewing the SD literature extensively. Finally, we conceptualize the variables and their behaviors by developing CLDs to capture CLVSC.

Description of system dynamics approach and causal loop diagrams

When making any critical choice, observation or modification, a systems approach entails understanding and addressing the entire system. The first and most important stage in a systems approach is to sketch up a broad picture of the whole system. However, comprehending a complex system with several components might be challenging. The direct and instantaneous one-way cause-and-effect links may be obvious, while other effects (such as those involving intermediaries, back-and-forth interactions among all stakeholders and delays) may not be apparent (Lee *et al.*, 2017). Thus, CLDs,

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qualitative models of SD, are used to capture all the effects that are difficult to foresee (Kontogiannis, 2021). Therefore, we create conceptual CLDs that address the challenges in the VSC. In our approach, similar to Kontogiannis (2021), we first develop several qualitative but quantifiable SD CLDs as the following:

- compartmental epidemic model of disease transmission that addresses the vaccine shortage (Paul and Venkateswaran, 2017);
- VSC that balances demand-supply while addressing the cold chain constraints;
- CLVSC that addresses security and sustainability challenges; and
- CLVSC with transshipment operations. Next, we incorporate all these models into a combined model to capture the dynamic replenishment of vaccines in a closed-loop environment (See Appendix 2 for table descriptions).

Conceptual causal loop diagrams

In this study, we use CLDs as conceptual modeling components to describe the conceptual feedback structure and better understand VSC behavior. CLDs can reveal feedback mechanisms and leverage points in a system. We adopt Sterman's (2000) stock management structure to develop CLDs and use Vensim software to draw CLDs. CLDs can be expanded further into stock and flow diagrams by applying differential equations. CLDs' feedback loops are developed by causal links among components of reality (Größler *et al.*, 2008). Two feedback loop types are used: balancing (negative) and reinforcing (positive) loop. Each arrow in the CLD represents a causal link or cause and effect relationship between the independent (the variable at the tail of the arrow) and the dependent variable (the variable at the head of the arrow). The positive (+) and negative (−) signs near the arrowhead indicate the direction of the cause-and-effect relationship. A pair of parallel lines imply a delay between the cause and effect. A reinforcing loop enhances the change (increase/decrease → increase/decrease) and creates a growing effect over time. Yet, a balancing loop opposes the change (increase/decrease → decrease/increase) and completes the balancing act over time (Sterman, 2000; Kamath and Roy, 2007). The variables in the boxes express the accumulated quantities (i.e. stocks), dashed arrows show the flow of information and solid arrows indicate the flow of physical goods.

SIR model

The SIR model (Sterman, 2000) is considered one of the most widely used SD models in the health-care domain that can be applied to any infectious disease (Darabi and Hosseinichimeh, 2020). SD modelers keep SIR as the core model and expand it with different levels of complexity and additional feedback loops. The SIR model, developed by Sterman (2000) based on Kermack and McKendrick's (1927) epidemic model, splits the population into three groups:

1 Susceptible Population (S).
2 Infectious Population (I).
3 Recovered (R).

Thus, the SIR model relaxes the second assumption of the SI model by including a balancing (negative) recovery loop. The recovery loop depicts that infected people only stay infected for a specific time, recover and establish long-term immunity. This represents the idea of herd immunity (Randolph and Barreiro, 2020), which is depicted by the recovery loop: the higher the number of infected people, the higher the recovery rate and the lower the number of remaining infected people. The SIR model depicts that when infectious people contact at a certain rate (*Contact Rate* [*CR*]) with susceptible people, the number of infectious people increases (contagion loop) by the *Infection Rate* (*IR*) (total number of contacts) while the number of susceptible people decreases (depletion loop). *Infectivity (IF)* represents the likelihood of a person contracting an infection, as not every contact with an infectious person results in infection. The *Average Duration of Infectivity* (*D*) is defined as the average length of time people are infectious with the assumption that each person's recovery time is different (some people recover in a short time, but for others, it takes longer), but as people recover, the population of infectious people will decrease exponentially. If the *IR* is lower than the *Recovery Rate* (RR), the infectious population will decline. When the infectious population declines, the *IR* declines. Therefore, the infectious population decreases to zero before the disease transmits to the entire population.

SIV model

Figure 2 depicts our integrated SIV model adopted from Paul and Venkateswaran's (2017) integrated supply chain and epidemics model. In our model, instead of *R and RR*, we use *Vaccinated Population (V) and Vaccination Rate (VR)*.

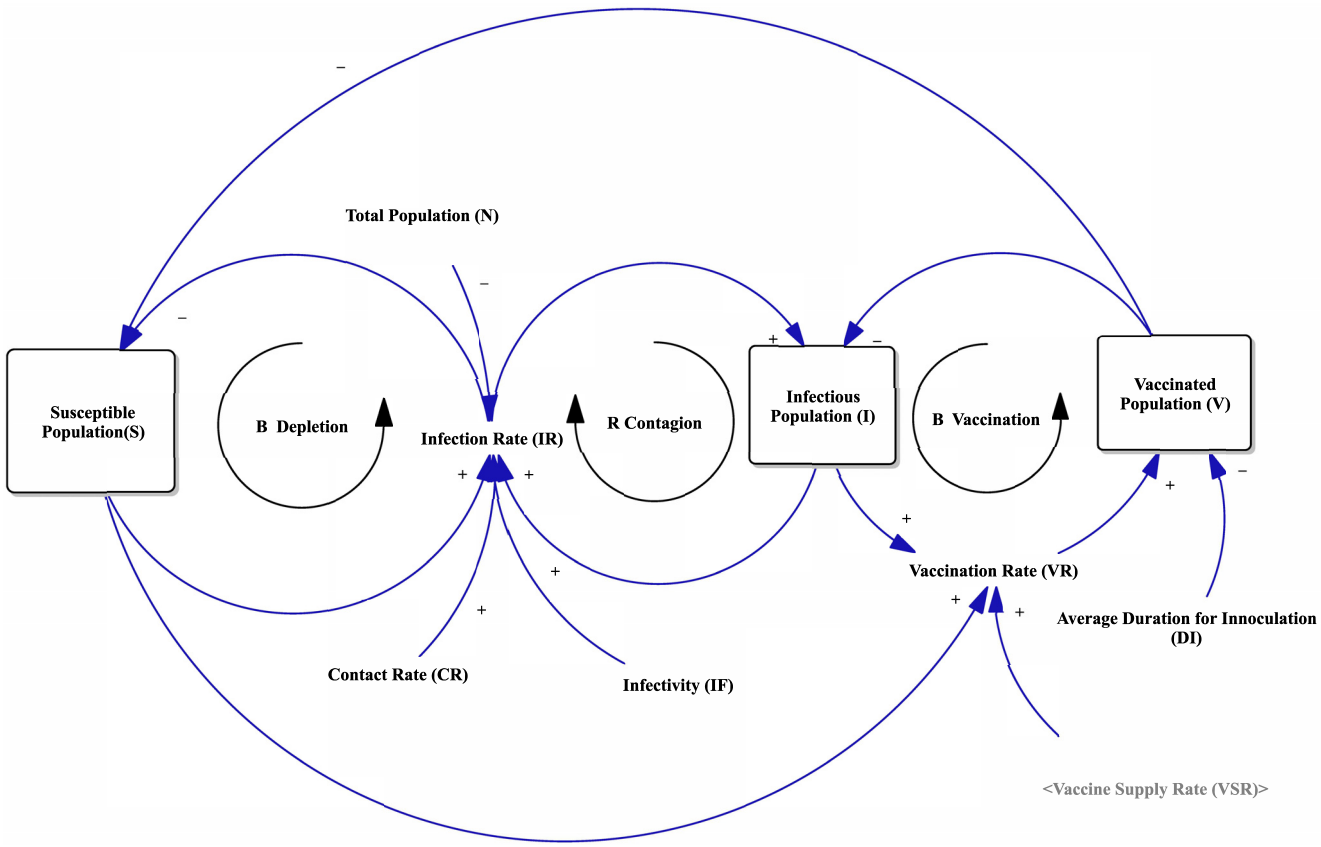
The *Average Duration of Inoculation (DI)* is the average length of time people are inoculated with the assumption that each person's inoculation time is different, but as people are inoculated, the population of infectious people will decrease exponentially. If the *IR* is lower than the *VR*, the infectious population will decline. When *I* declines, the *IR* also declines. Furthermore, vaccinated people gain immunity for a certain period and become susceptible to COVID-19 and its variants (*Vaccinated Population* [*V*] increases the *S*). In reality, susceptible people do not have to become infected to get vaccinated. Instead, they receive vaccinations to reduce the likelihood of getting infected. Therefore, in our model, *S* increases *VR*. We integrate *VR* into our CLVSC.

The supply rate for a vaccine is generated from the VSC model [adopted from Gonul Kochan *et al.*'s (2018) hospital supply chain model] and integrated into the SIV model.

Vaccine supply chain order fulfillment

Vaccination site CLD (Figure 3) begins with the *Vaccine Demand* (*VD*), the population eligible for receiving vaccines, which leads to a rise in *Vaccine Order Rate* (*VOR*). When there is no available inventory in stock to fulfill orders promptly, *VOR* leads to an increase in *Vaccine Order Backlog* (*VOB*) which refers to unsatisfied/unfulfilled orders (Sterman, 2000; p. 724; Venkateswaran and Son, 2007; Wilson, 2007). A rise in *VOB* leads to an increase in *Vaccine Delivery Delay (VDD)*, the average delay between the placement and the receipt of the vaccination order. *VDD* becomes equal to the *Target Delivery Delay* (*TDD*), which refers to the vaccination site's target for the interval between placement and receipt of vaccine

Figure 2 SIV model



Note: The connected variables between models are shown as "Gray Shadow Variables" to simplify the overall model

orders (Sterman, 2000; p. 725) when the *Desired Supply Rate for Vaccine* (*DSRV*) (the vaccination site's target supply rate) is equal to the *Vaccine Supply Rate* (*VSR*). *DSRV* is calculated as the ratio of *VOB* and *TDD* and confirms that the vaccines are filled within the vaccination site's *TDD* time. *TDD* is determined by the vaccination site to meet the *VD* on time. An increase in *TDD* increases *DSRV* while decreasing *VOB*. A rise in *VOB* also leads to an increase in *DSRV*.

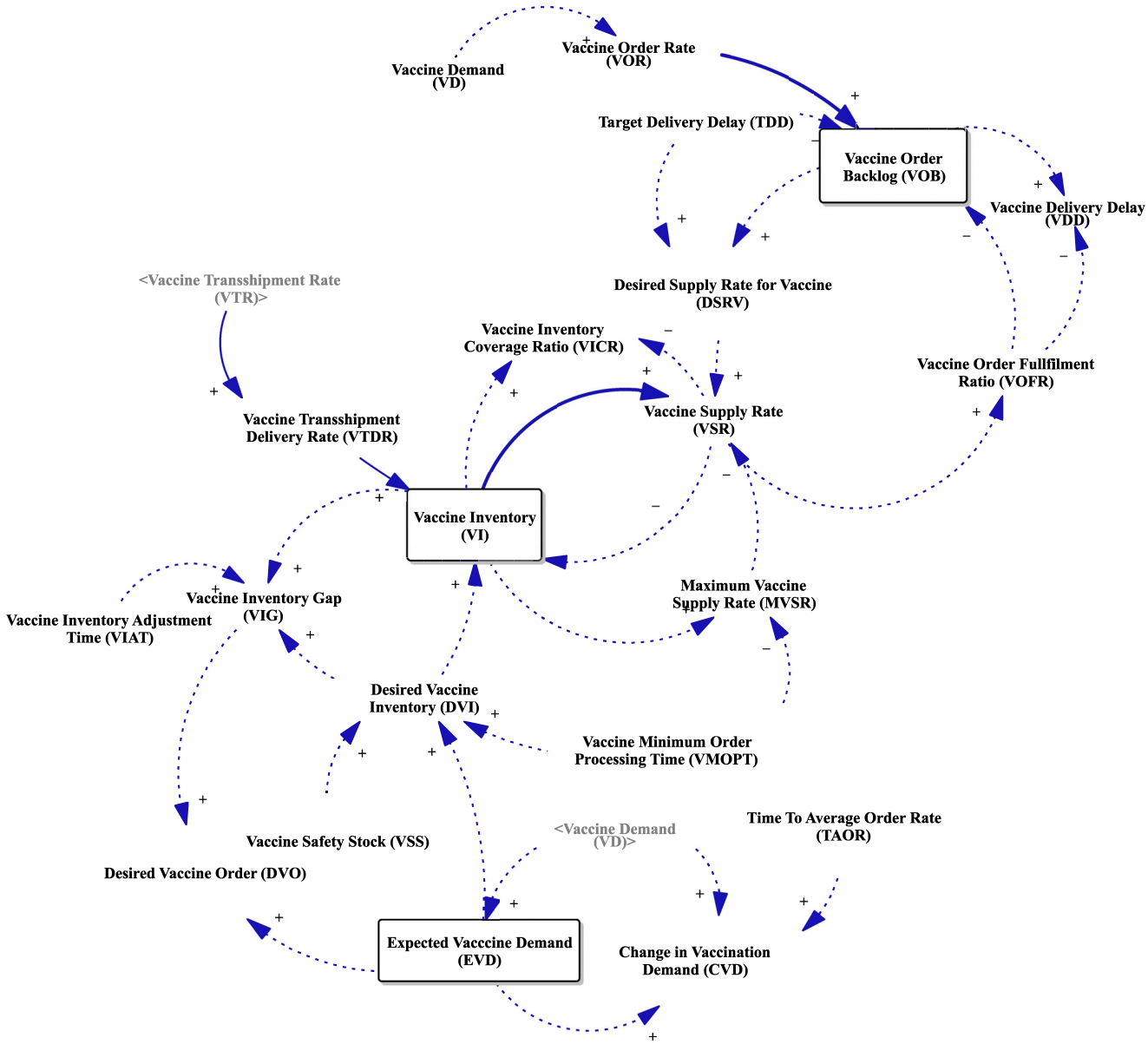
DSRV leads to an increase in the *VSR* when the *Vaccine Inventory (VI)* in stock is sufficient. *Vaccine Inventory (VI)* refers to the vaccine inventory on hand at each vaccination site and accumulates vaccines shipped from manufacturers/distributors and transshipped from other vaccination sites. Inventory in stock is used to supply the vaccination demand at the current vaccination site and supply vaccination sites in need of vaccines. Consequently, *VSR* leads to an increase in the *Vaccine Order Fulfillment Ratio (VOFR)* (Kamath and Roy, 2007; Venkateswaran and Son, 2007). Once the orders are fulfilled within time, *VOFR*, *VOB* and *VDD* decrease.

Inventory control

Adequate *VI* in stock raises the vaccination site's *Maximum Vaccine Supply Rate* (*MVSR*). The *MVSR* is described as the maximum number of supplies given the *VI* in stock and *Vaccine Minimum Order Processing Time* (*VMOPT*). *VMOPT* refers to the amount of time it takes between the order being placed and shipped. Thus, a rise in *VMOPT* leads to a decrease in *MVSR*. *MVSR* decreases the *VSR* since a vaccination site cannot supply more than *MVSR*. Contrarily, a rise in *VSR* leads to a decrease in *VI*. It is critical to determine whether a *VSR* is adequate to meet with the *VD* to avoid stockouts. *Vaccine Inventory Coverage Ratio* (*VICR*) refers to the number of days the vaccination site could supply at the current *VSR* given *VI* in stock, revealing the service level of the vaccination site. The lower the *VICR*, the more a vaccination site desires a rise in the *VI* level to meet with the *VD*. The *Desired Vaccine Inventory* (*DVI*) is the volume of inventory required to keep a vaccination site's desired service level of full and dependable delivery. *DVI* is estimated by the *Expected Vaccine Demand* (*EVD*) and depends on the vaccination site's *Vaccine Safety Stock* (*VSS*) and *VMOPT*. *VSS* is challenging due to the highly perishable nature of the vaccines. Cold storage temperature and wastage are the most significant constraints.

EVD and *DVI* rise in response to an increase in *VD* over time (Georgiadis *et al.*, 2006). The vaccination site reviews *Change in Vaccination Demand* (*CVD*) when setting the *DVI* level. *CVD* refers to the discrepancy between *EVD* and the vaccination site's *VOR* over a period determined by the *Time to Average Order Rate* (*TAOR*). The *VD* information is used to calculate *EVD* by smoothing the demand figures with the previous period's perceived demand. A vaccination site wishes to

Figure 3 Order fulfilment inventory control and order placement at the vaccination site



Note: The connected variables between models are shown as "Gray Shadow Variables" to simplify the overall model

maintain its *DVI* equal to the *EVD* (Venkateswaran and Son, 2007). The *DVI* level leads to an increase in the *Vaccine Inventory Gap* (*VIG*) and the disparity between *DVI* and *VI*. *Vaccine Inventory Adjustment Time (VIAT)*, the time required to take the inventory to the desired level, corrects *VIG* over a period of time.

Order placement

As the *VIG* increases, *Desired Vaccine Order* (*DVO*) increases (Wilson, 2007). *DVO* translates to the *Vaccination Site's Order Rate* (*VSOR*) in the manufacturer/distributor and transshipment echelon. Therefore, *DVO* results in shipments to the vaccination site denoted as *Vaccine Transshipment Rate* (*VTR*), which translates into *Vaccine Transshipment Delivery Rate* (*VTDR*). A rise in *VTDR* increases the *VI* and the service level, called *Vaccine Inventory Coverage Rate* (*VICR*). In the distributor/manufacturing echelon, order fulfillment, inventory control and order placement processes remain the same as in the vaccination site echelon (Gonul Kochan *et al.*, 2018), which is not shown here.

In the VMI setting, the forecasted *VD is* communicated to all vaccination sites' suppliers, including manufacturers and distributors. Vaccination sites no longer place orders with distributors/manufacturers. Therefore, there are no or minimal order backlogs on vaccination sites (Wilson, 2007). The vaccine order information is automatically sent to the manufacturer/distributor based on the *DVO*, *EVD* and *VIG*.

Production

CLDs in Figure 4 are mainly adapted from Gonul Kochan *et al.* (2018). The manufacturer's CLD (Figure 4) starts with *DVO*, which triggers an increase in *Expected Vaccination Site Demand* (*EVSD*). As *EVSD* rises, the manufacturer's *Desired Production (DP)* increases. *Production Release Rate* (*PRR*) increases as *DP* rises (Venkateswaran and Son, 2007) and *Work in Process Inventory* (*WIPI*) increases, respectively (Georgiadis *et al.*, 2006). When production begins, the difference between *PRR* and *Production Completion Rate* (*PCR*) is accumulated in *WIPI*, and *WIPI* increases the *PCR*. The pending production line, or *WIPGap (WIPG)*, is the difference between the *Desired WIP* (*DWIP*) and *WIP Adjustment Time* (*WIPAT*) (Sterman, 2000; p. 714). *WIPG* adjusts the *PRR* to keep up with *WIPI* and the *Manufacturer's Inventory* (*MI*) at the *DWIP* level. *Manufacturing Lead Time (MLT)* increases the *DWIP* (Venkateswaran and Son, 2007) due to the third-order delay, resulting in a drop in *PCR*. The *PCR* leads to an increase in *MI*. *The MI Gap (MIG)* is reduced when the MI level is sufficient (Wilson, 2007). The lower the *DP* level, the lower the *MIG*, or vice versa. Increased *MI* levels also result in higher *Maximum Manufacturer Shipment Rate (MMSR)* and *MS Rate (MSR)*.

Closing the loop

We adopted Vlachos *et al.*'s (2007) SD CLD model to describe the reverse flow of VSC (Figure 5). *VI* at the end of their current *Vaccine Usage Duration (VUD)* (usage until expiration or expired) becomes *Used Vaccine (UV)* (used or expired vaccines). *VUD* depends on the vaccine's shelf life. *UVs* are either disposed of and lead to an increase in *Uncontrollable Vaccine Disposal (UVD)* or collected for reuse/recycling and lead to an increase in *Collection Rate (CR) and Collected Vaccines (CV)*, respectively. For instance, if opened, vials that still have doses inside can be stored for reuse. Furthermore, if vials are appropriately stored after usage, they can be recycled (Klemeš *et al.*, 2021).

Collection

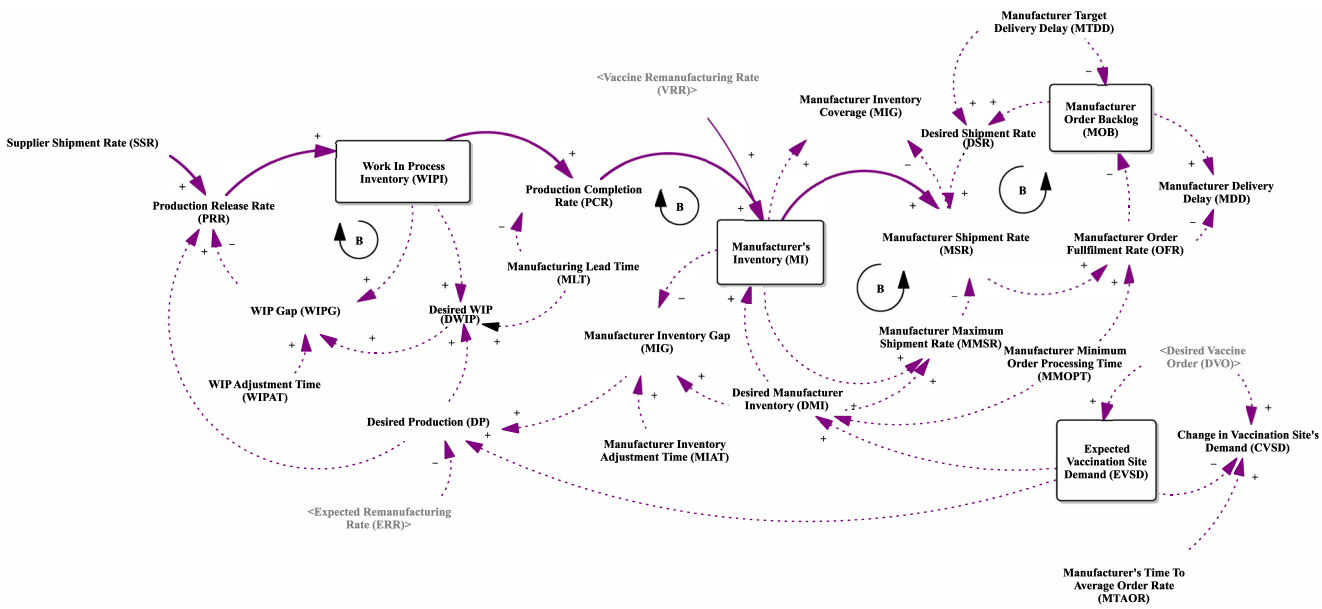
VCR increases the *CV* and relies on the *Collection Capacity (CC)* (e.g. truck capacity, cold storage capacity). *CV* is decreased by the number of vaccines either accepted after inspection (*Vaccines Accepted for Reuse* [*VAR*]) or rejected (*Vaccines Rejected for Reuse* [*VRFR*]). *Inspection Time (IT)* refers to the inspection being completed within a given time. *VAR* and *VRFR* increase as *IT* increases, which indicates that the inspection is performed. The inspection outcome (*VAR* or *VRFR*), which takes *IT*, is formed based on several reuses (remaining non-expired doses) and remaining shelf life, and the *Failure Percentage* (*FR*). *FR* refers to a small fraction, a percentage of failing an inspection. Vaccine Vial Monitors can reduce the inspection failure percentage as these are small, color-changing labels that are affixed to the vials. The color-changing is governed by temperature changes and is essential in supporting ideal storage monitoring vaccine vials [VII].

Remanufacturing

If the *Remanufacturing Capacity* (*RC*), which limits the *Vaccine Remanufacturing Rate* (*VRR*), is appropriate, the supply of *Reusable Vaccines* (*RV*) can be used for remanufacturing. *Controllable Vaccine Disposal* (*CVD*) has been devised to prevent an unending buildup of reusable products by draining them if they remain unused for some time (*Reusable Stock Keeping Time* [*RST*]).

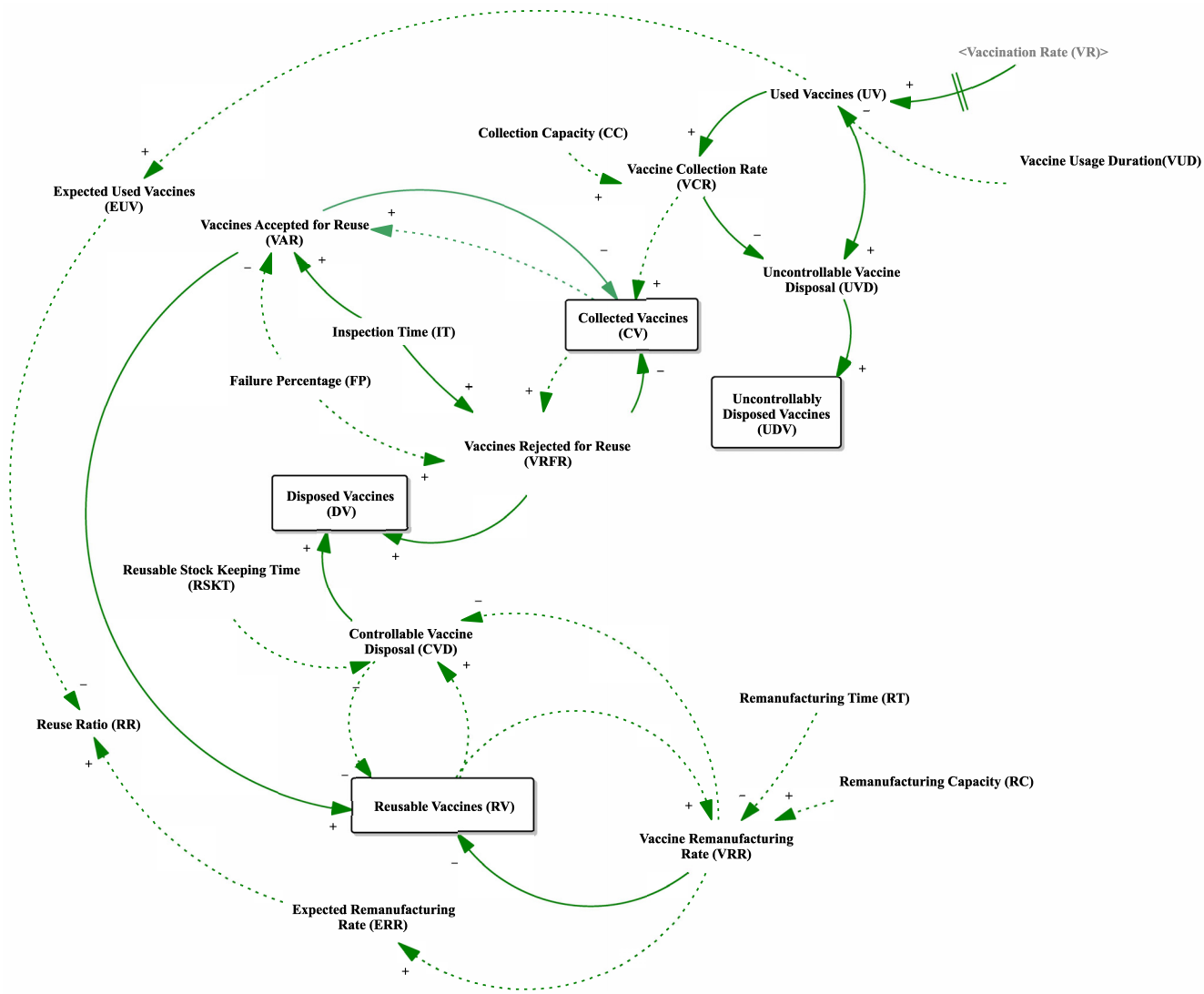
The *Reuse Ratio* (*RR*), defined as the ratio of the *Expected Remanufactured Rate* (*ERR*) to the number of *Expected Used Vaccines* (*EUV*), represents the remanufacturing/reuse activities. There are currently no take-back obligations; however, even without the regulations, given the risks associated with improper disposal, vaccines and packaging

Figure 4 Production at the manufacturing site



Note: The connected variables between models are shown as "Gray Shadow Variables" to simplify the overall model

Figure 5 The reverse flow of VSC



Note: The connected variables between models are shown as "Gray Shadow Variables" to simplify the overall model

should be collected back. In our model, *ERR* decreases the *DP*. We omit production capacity in our model, as our focus is on vaccine waste and distribution.

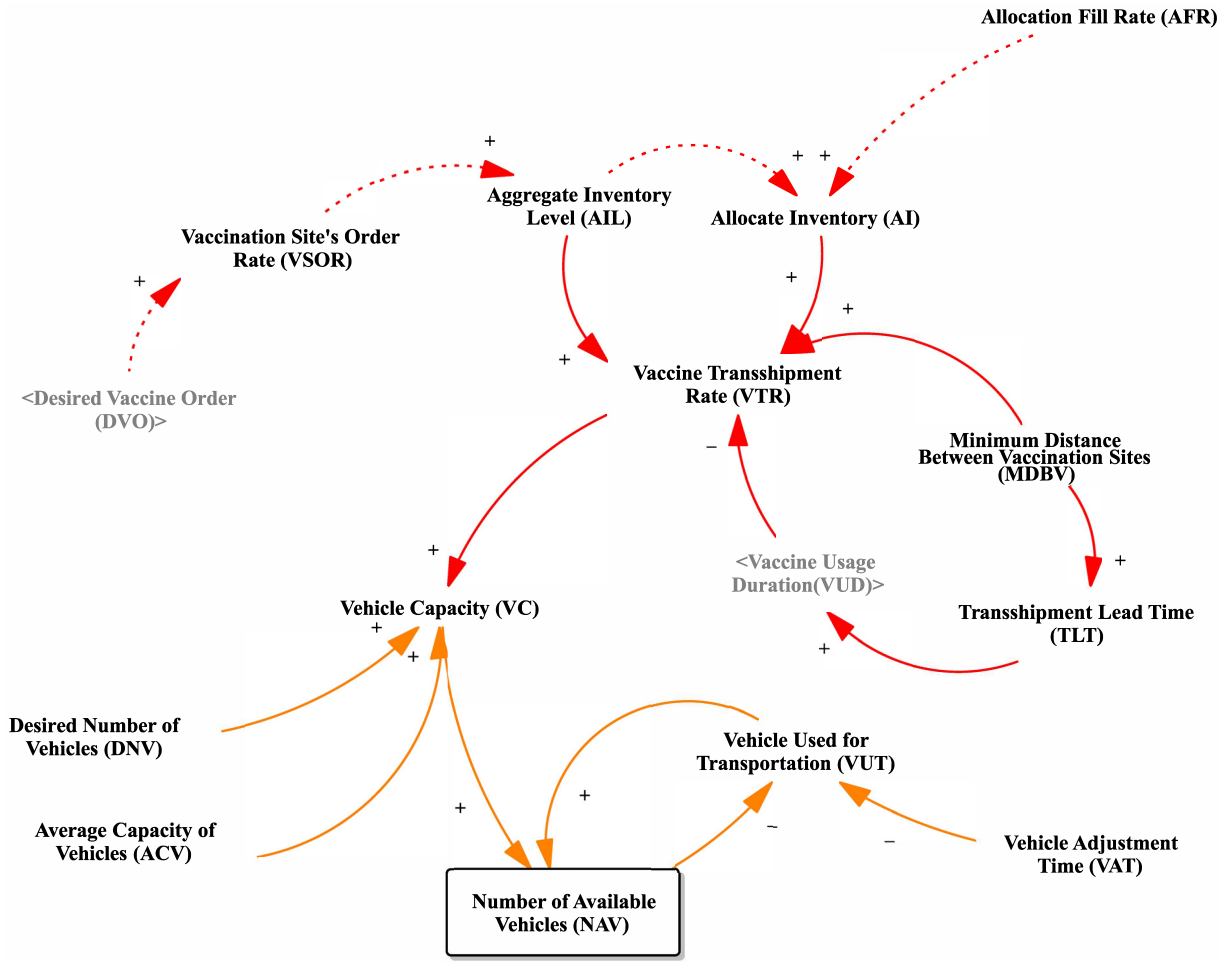
Transshipment

Figure 6 presents a visual representation of the proposed model of transshipments. We suggest using the VMI system to allow for central inventory decisions. Specifically for the vaccine sites, transshipment operations are integrated via VMI, creating a virtual pool of inventory called *Aggregate Inventory Level (AIL)* displays available inventory levels on each vaccination site.

There are various factors to consider while managing transshipments, such as the timing of transshipments, the allowable number of transshipments within a timeframe, the sender and receiver location pairings and the coordination of the transshipment movements (Archibald *et al.*, 1997; Çömez-Dolgan and Fescioglu-Unver, 2015).

The VMI system is designed to use real-time supply and demand data for vaccine allocation decisions between vaccination sites based on available inventory at each vaccine site via *Allocation Inventory* (*AI*).The decisions for the transshipments will be made by considering the potential excess inventory based on *Allocation Fill Rate* (*AFR*) (Botha *et al.*, 2017), the remaining shelf life of the vaccine doses, *VUD*, and the need for inventory in vaccine sites that are within reach depending on *Minimum Distance Between Vaccination Sites* (*MDBV*) given the remaining shelf life. As the time window for the transshipment operations is narrow, as indicated by *Transshipment Lead Time* (*TLT*), it is critical for the decisions and the operations to be agile and accurate. As *AIL* increases, the *AI* decisions lead to a rise in *Vaccine Transshipment Rate* (*VTR*). Transshipments made between equivalent locations in the supply chain are called lateral transshipments (Paterson *et al.*, 2011). As Tlili *et al.* (2012) note, there are two types

Figure 6 Transshipment at VSC



Note: The connected variables between models are shown as "Gray Shadow Variables" to simplify the overall model

of transshipment: emergency and preventive. Emergency transshipments offer inventory replenishment in an actual stockout case, whereas preventive transshipments are routine inventory redistributions (Tlili *et al.*, 2012). In our model, we mainly focus on the latter.

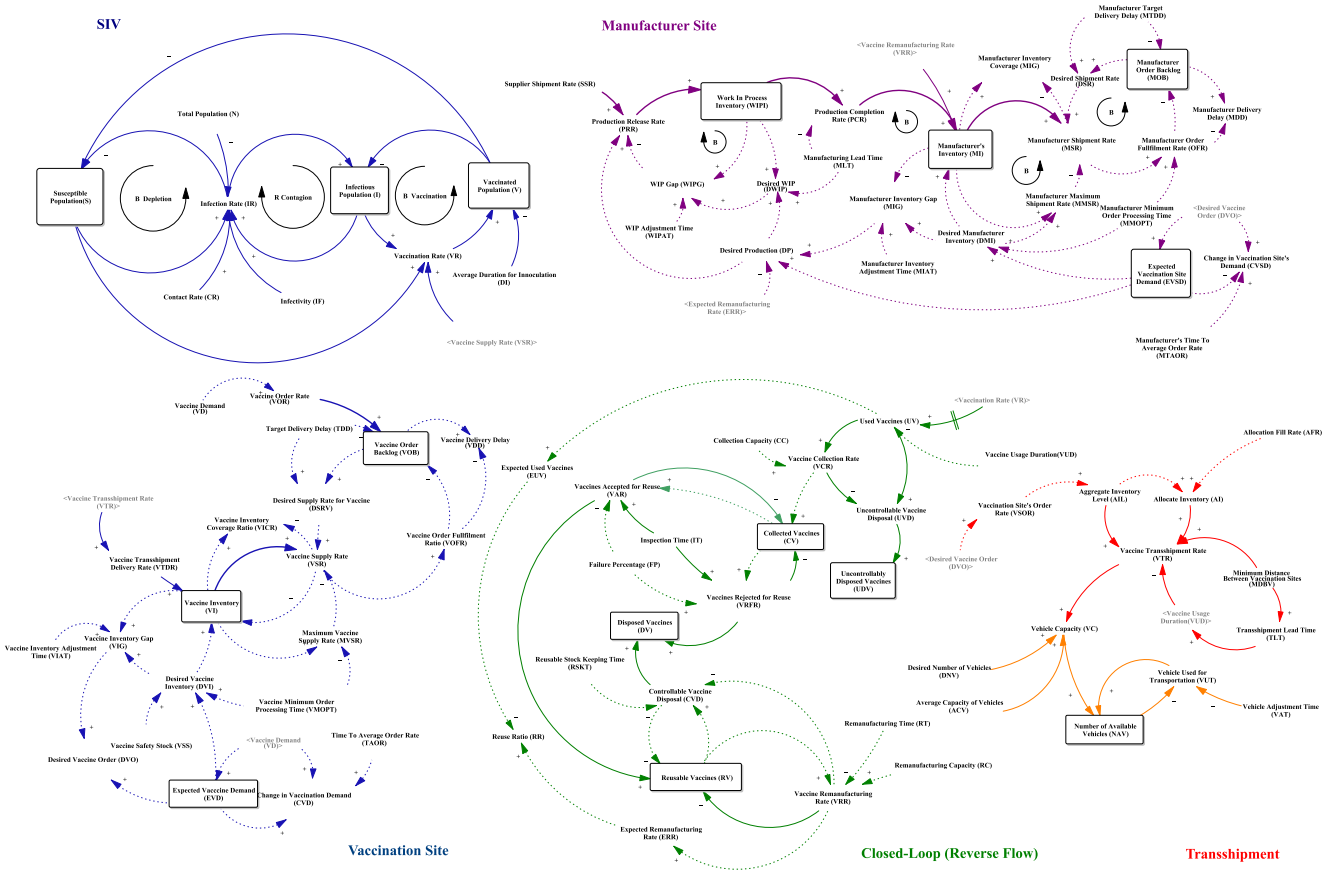
Vehicle capacities are also essential due to cold chain requirements for vaccines. Therefore, we adopted vehicle capacity planning from Rathore *et al.* (2021). Both *VTR* and *Desired Number of Vehicles* (*DNV*) increase the Vehicle Capacity (*VC*), and *VC* should not exceed the Average Capacity of Vehicles (*ACV*). An increase in *VC* requires more vehicles, increasing the *Number of Available Vehicles* (*NAV*). *NAV* refers to the discrepancy between *VC* and *Vehicles Used for Transportation* (*VUT*). The more *NAV* for transshipment, the less the *VUT*, and vice versa. Similarly, the time to prepare vehicles, Vehicle *Adjustment Time* (*VAT*), decreases *VUT*.

The overarching model of closed-loop vaccine supply chain

Figure 7 depicts the overarching model of CLVSC. In the literature, most quantitative SD models focus on intra-organizational behavior and do not capture the holistic view of the supply chains (Kontogiannis, 2021). This focus refrains from examining the underlying structure and identifying potential interactions. Therefore, it is essential to incorporate multiple models to depict supply chain operations entirely. This paper builds a qualitative overarching CLD for COVID-19 VSC that contains SIV, vaccination site, manufacturer site, closed-loop and transshipment operations (Figure 7).

CLVSC starts with *VD* at the vaccination site model. As *VI* depletes to supply *VD*, the vaccination site's *DVO* is automatically triggered in the VMI system and the order information is transferred to all vaccination sites. The connection between the vaccination site model (Figure 3) and the transshipment model (Figure 6) is made via *DVO*. As *DVO* increases, *VSOR* increases in the transshipment model. In the transshipment model, inventory level information of all vaccination sites are aggregated in the system (*AIL*), the system allocates inventory (*AI*) and matches vaccination sites' inventory needs based on the minimum distance (*MDBV*). Based on the vehicle transportation capacity (*VC*), vaccines are transshipped to vaccination sites (*VTR*). The vaccine sites supply the demand (*VSR*). If the vaccines expire due to their *VUD*, closed-loop operations take place. At the same time, *VSR* increases *VR* in the SIV model. As *VR* increases, *UV* increases in

Figure 7 Overarching model



Note: The connection variables between models are shown as "Gray Shadow Variables" to simplify the overall model

the closed-loop model. Collected *UV*s are inspected; if they are accepted for reuse (*VAR*), *VAR* increases *RV*. *RV* increases *VRR* and connects to the manufacturer site. At the manufacturer site, *VRR* increases *MI*, and *ERR* increases *DP*. Once the *MI* increases, manufacturers ship vaccines (*MSR*) to vaccination sites based on the information of *DVO* in the VMI system (Appendix 3 presents the structure of the major feedback loops).

Discussion

While epidemics are in decline, vaccinations are instrumental in fending off additional waves (Lee *et al.*, 2010). Applying this thinking to the COVID-19 pandemic, even when numbers of infected individuals and fatalities may decrease, efforts to establish an effective VSC are needed to keep fighting against new waves and variants. Additionally, the capabilities built for the battle against the COVID-19 pandemic would be extremely valuable for future epidemics and pandemics.

Ad hoc systems have been proposed to address inventory shortages (Lee *et al.*, 2010). Nevertheless, *ad hoc* systems are problematic in the overall design owing to their inconsistency and the inability to monitor and manage such efforts. Our model resolves this issue by offering a flexible approach that can still be controlled, manageable and monitored.

Given the unique challenges of VSCM, establishing and maintaining well-functioning, consistent and reliable databases is extremely critical. Especially in the case of pandemics, timely and accurate geographic data are crucial. However, due to privacy concerns, these data are not usually reported or are not reported with precision. Thus, establishing more consistent, reliable and secure databases is essential (Mast *et al.*, 2021).

Sustainability intersects with individual and society's well-being. For example, Griffith (2006) posits that human capital is essential for supply chain success. Supply chain members can use an assessment and matching strategy to place individuals in positions where they would create the most value. However, one of the complex impacts of the COVID-19 pandemic has been workplace changes (Kniffin *et al.*, 2021), and as Alam *et al.* (2021) discuss, only through proper vaccine demand forecasting people can resume work and contribute to economic growth.

The transshipment element incorporated in the conceptual model was essential to be included because of the significant amount of vaccine doses wasted at the vaccination sites. Additionally, in the face of potential stockouts in any vaccination site, especially in more rural areas where alternative locations may not be easily accessible, it is more efficient for vaccination sites to transship vaccine inventory instead of asking people to travel to other locations to receive vaccines.

The circumstances of the pandemic have been challenging to manage. The inherent complexities and poor management have resulted in numerous negative impacts on society, the environment and the economy. The main challenges of the VSCM are the lack of coordination in vaccine supply operations and waste management issues. Although effective management of the COVID-19 VSC requires collaboration throughout the SC, we have observed a lack of collaboration in the current VSCM systems. In addition, a thorough literature review has revealed a lack of research that describes a holistic approach to vaccine supply chain operations (Fadaki *et al.*, 2022). In our study, we propose a model that would integrate components allowing a more holistic view of the VSC amidst a pandemic. To the best of our knowledge, our research is the first to propose a model that integrates VMI, transshipment and a closed-loop structure to the VSC.

The VMI helps monitor supply throughout the system and allows the centralization of inventory decisions. Transshipments enable the inventories to be balanced among vaccination sites and provide opportunities for decreasing wasted vaccines. Additionally, the closed-loop structure allows for monitoring vaccinations and relevant packaging at the end-of-life stage, creating two main advantages:

1 decreasing vaccine thefts and counterfeit vaccines; and
2 decreasing negative environmental impact.

Conclusion

The COVID-19 pandemic introduced unprecedented challenges related to factors such as increased global connectivity. Supply chain disruptions and management challenges cause further unrest during pandemic mitigation efforts. Although significant strides have been made in establishing a functioning COVID-19 VSC, some threats have been observed that threaten the safekeeping and delivery of vaccines.

Our paper contributes to the literature by enhancing the understanding of health-care delivery challenges and sustainability during the pandemic through a comprehensive closed-loop SD model designed for VSC.

We propose that establishing a closed-loop structure for the VSC is essential to ensure wasted vaccines are accounted for, monitored and recollected safely. However, one other major objective should be to minimize vaccine doses wasted in the first place. As the number of doses required globally cannot be manufactured quickly, the manufactured doses must be used and not wasted within their shelf life. Therefore, the transshipment operations are instrumental in establishing a way for an agile last-mile vaccine logistics operation. In addition, establishing accurate and reliable real-time data-based information systems is vital for the suggested VSC to work effectively.

The model addresses the issues of negative environmental and societal impacts. The environmental impact is improved, as waste is proposed to be collected and disposed of properly. The societal impact is improved as the potential for vaccine dose theft is diminished, and agile transshipment operations can provide more equitable vaccine distribution.

The model proposed in this study contributes to the literature by integrating new elements into the traditional health-care models, which are essential for handling the case of pandemics.

Limitations and future research

We have built a conceptual model; however, testing it with numeric examples would be beneficial. Additionally, we focused on the US VSC, recognizing that vaccine operations look very different depending on location. Therefore, if applied in other settings, the model may need to be adapted according to the different circumstances as required by the different locations. The biggest challenge of VSCs, especially amidst a pandemic, is establishing a global supply chain structure. Therefore, the issue of data and information system inconsistencies only worsens when the VSC is considered on a global scale. Consequently, when the global VSC is studied, there should be intermediary steps to evaluate the communication of distinct systems. Therefore, the model proposed in this study might not apply to other settings.

We would also like to offer some avenues to guide future research areas. It would be beneficial to study transshipment operations on an international scale for future research. As Alam *et al.* (2021) note, the inequalities on the global scale increased in the face of inequitable access to vaccines. Therefore, given the differences in opportunities and the capabilities of supply chains, studying the effects of such a strategy in an international setting so that countries within travel distance can support each other's vaccine availability.

Klemeš *et al.* (2020) point out the insufficient waste handling/treatment capacities and note that it is crucial to build capabilities to safely handle the vast amount of waste generated in the VSC. With our proposed closed-loop design, we are addressing the issues of material shortages, safety concerns and diverting waste from landfill. However, for this to work, capacities still need to be improved. Therefore, future work should also include capacity considerations.

Future research could also investigate the impacts of thermostable vaccines on VSCs nationally and, especially, globally. Cold chains are challenging to maintain, especially given the availability and potential disruptions in the global supply chain. Making vaccines thermostable is a possible solution for decreasing cold chain dependency (Chen and Kristensen, 2009). Research for developing thermostable COVID-19 vaccines has been in development (Zhang *et al.*, 2020). As the viability and availability of these vaccines are observed in different countries, researchers can build on the assumptions of vaccines being thermostable into their models. Thus, cold chain constraints could be relaxed along with the relevant time constraints for storing vaccines.

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Appendix 1

Table A1 Abbreviations list

Abbreviations List	
Causal Loop Diagrams	CLD
Centers for Disease Control and Prevention	CDC
Closed-Loop Vaccine Supply Chain	CLVSC
Collaborative Planning	CP
Collaborative Planning, Forecasting, and Replenishment	CPFR
Electrical and Electronic Equipment	EEE
Electronic Data Interchange	EDI
Electronic Supply Chain Management Systems	e-SCM
Information Technology	IT
Sustainable Supply Chain Management	SSCM
System Dynamics	SD
Vaccine Supply Chain Management	VSCM
Vaccine Supply Chains	VSC
Vaccine Tracking System	VTrckS
Vaccine Vial Monitors	VVM
Vendor Managed Inventory	VMI
World Health Organization	WHO

Appendix 2

Table A2 Variable notation and descriptions

Variables	Notation	Short description of variables
SIR and SIV Loops		
Susceptible Population	S	The number of people susceptible to infection
Infectious Population	I	The number of susceptible people get infected
Recovered Population	R	The number of people recovered from infection
Contact Rate	CR	The number of Infectious people contact with susceptible people
Average Duration of Infectivity	D	The average length of time people are infectious
Infection Rate	IR	Total number of contacts
Infectivity	IF	The likelihood of a person contracting an infection
Recovery Rate	RR	Total number of people recover from an infection
Vaccinated Population	V	The number of vaccinated people
Vaccination Rate	VR	Total number of vaccinated people
Average Duration of Inoculation	DI	The average length of time people are inoculated
VSC Order Fulfillment Loop		
Vaccine Demand	VD	Population eligible for receiving vaccines
Vaccine Order Rate	VOR	The total number of vaccine orders for vaccination
Vaccine Order Backlog	VOB	Unsatisfied/ unfulfilled vaccine orders
Desired Supply Rate for Vaccine	DSRV	Vaccination site's target supply rate
Target Delivery Delay	TDD	A certain amount of time required to fill the vaccine orders
Vaccine Inventory	VI	Vaccine inventory on hand
Vaccine Supply Rate	VSR	The total number of vaccine orders supplied
Vaccine Order Fulfillment Ratio	VOFR	A function of maximum vaccine supply rate and desired vaccine supply rate
Vaccine Delivery Delay	VDD	The average delay between the placement and the receipt of the vaccination order
Inventory Control Loop		
Maximum Vaccine Supply Rate	MVSR	The maximum number of supplies given the VI in stock and VMOPT
Vaccine Minimum Order Processing Time	VMOPT	The amount of time it takes between the vaccine order being placed and shipped
Vaccine Inventory Coverage Ratio	VICR	The number of days the vaccination site could supply (service level of the vaccination site)
Desired Vaccine Inventory	DVI	The volume of inventory required to keep a vaccination site's desired service level of full and dependable delivery
Expected Vaccination Demand	EVD	Expected/forecasted demand
Vaccine Safety Stock	VSS	Additional vaccine inventory in stock to prevent stockouts
Change in Vaccination Demand	CVD	The discrepancy between EVD and the vaccination site's VOR over a period determined by the TAOR
Time to Average Order Rate	TAOR	The time between vaccine orders
Vaccine Inventory Gap	VIG	The disparity between DVI and VI
Vaccine Inventory Adjustment Time	VIAT	The time required to take the inventory to the desired level
Order Placement Loop		
Desired Vaccine Order	DVO	The vaccination site's desired vaccine order
Vaccination Site's Order Rate	VSOR	The total number of vaccine orders placed
Vaccine Transhipment Rate	VTR	The number of vaccines shipped to vaccination site via transshipment
Vaccine Transhipment Delivery Rate	VTDR	The total number of vaccines delivered to vaccination site via transshipment
Production Loop		
Desired Production	DP	Desired number of vaccines to be produced
Expected Vaccination Site's Demand	EVSD	Expected/forecasted vaccination site's demand
Production Release Rate	PRR	The total number of vaccines released for manufacturing
Work In Process Inventory	WIPI	The number of vaccines accumulated by difference between PRR and PC
Product Completion	PC	The total number of vaccines produced
Work in Process Gap	WIPG	The pending production line (the difference between DWIP and WIPAT)
Desired Work In Process	DWIP	Desired number of vaccines to be accumulated in the production line
Work In Process Adjustment Time	WIPAT	The time it takes to modify WIPG in line with the desired level
Manufacturing Lead Time	MLT	The average cycle time for the vaccine production

(***continued***)

Table A2

Variables	Notation	Short description of variables
Manufacturer's Inventory	MI	Manufacturer's vaccine inventory on hand
Manufacturer's Inventory Gap	MIG	The disparity between DMI and MI
Maximum Manufacturer Shipment Rate	MMSR	The maximum number of shipments given the MI in stock and MMOPT
Manufacturer Shipment Rate	MSR	The total number of vaccines shipped from Manufacturer
Manufacturer Minimum Order Processing Time	MMOPT	The amount of time it takes between the vaccine order being placed and shipped at the manufacturer
Closing the Loop		
Vaccine Usage Duration	VUD	Vaccine usage until expiration or expired vaccines which depends on the vaccine's shelf life
Used Vaccine	UV	Used or expired vaccines
Uncontrollable Vaccine Disposal	UVD	The flow of used vaccines to disposal due to the limited collection capacity
Uncontrollably Disposed Vaccines	UDV	A variable that accumulates the uncontrollably disposed vaccines
Collection		
Vaccine Collection Rate	VCR	The flow of used vaccines to the collection and inspection facilities
Collected Vaccines	CV	The inventory of collected reused vaccines
Collection Capacity	CC	The maximum volume of vaccines handled by the collection and inspection facilities per week
Vaccines Accepted for Reuse	VAR	The flow of used products that have passed inspection and are appropriate to be remanufactured
Vaccines Rejected for Reuse	VRFR	The flow of used products that have not passed inspection and are appropriate to be remanufactured
Inspection Time	IT	The time inspect calculated based on several reuses (remaining non-expired doses) and remaining shelf life
Failure Percentage	FR	A percentage of failing in inspection
Remanufacturing		
Remanufacturing Capacity	RC	The maximum volume of reused products that can be remanufactured per week
Vaccine Remanufacturing Rate	VRR	The flow of remanufactured vaccines
Reusable Vaccines	RV	The inventory of used products that passed inspection and are ready to be remanufactured
Controllable Vaccine Disposal	CVD	The flow of surplus stock of used vaccines to prevent costly accumulation if there is not enough remanufacturing capacity to handle them
Uncontrollable Disposal	UCD	The flow of used vaccines to disposal due to the limited collection capacity
Reusable Stock Keeping Time	RST	Unused vaccines for some time
Reuse Ratio	RR	The ratio of ERR to the number of EUV
Expected Remanufacturing Rate	ERR	The forecast of remanufacturing rate
Expected Used Vaccines	EUV	The forecast of used products
Vehicle Capacity		
Desired Number of Vehicles	DNV	The desired number of vehicles to transport vaccines
Average Capacity of Vehicles	ACV	The average amount of vaccines can be transported by vehicles
Vehicle Capacity	VC	The maximum vaccine transshipment rate that is restricted by ACV
Number of Available Vehicles	NAV	The discrepancy between VC and VUT
Vehicle Used for Transportation	VUT	The number of vehicles used for transshipment
Vehicle Adjustment Time	VAT	The time required to prepare the vehicles
Transshipment		
Vaccine Transshipment Rate	VTR	The total number of vaccines shipped from vaccine site *n* to vaccine site k
Aggregate Inventory Level	AIL	The total number of the available inventory across all vaccination sites
Allocate Inventory	AI	Allocation decision of inventory from available inventory stock at vaccination site *n* to vaccination site k based on vaccination site k's DVO, MDBV, and AFR
Allocation Fill Rate	AFR	If the vaccination site *n* has available inventory to allocate, the AFR score becomes one, else it is zero
Minimum Distance Between Vaccination Sites	MDBV	Ensures the minimum distanced vaccination site k is matched to vaccination site *n* to allocate vaccines
Transshipment Lead Time	TLT	The time that elapses between vaccine transshipment allocation and the delivery at vaccination site k

Appendix 3

The Structure of the Major Feedback Loops
Order Fulfillment at the Vaccination Site
VD + → VOR + → VOB + →VDD
VOB + → DSRV + → VSR + → VOFR − → VOB
TDD + → DSRV
TDD − → VOB
VOFR − → VDD
Inventory control at the Vaccination Site
VI + → MVSR − → VSR − → VICR
VMOPT − → MVSR − → VSR − → VI + → VICR
VSS + → DVI + →VIG
VMOPT + → DVI
EVD + → DVI + → VI + → VIG
VIAT +→ VIG
Order Placement
VTR + → VTDR + → VI + → VSR + → VICR
Production
DVO + → EVSD + → DP + → PRR + → WIPI + → PCR + → MI + → MSR
WIPI + → DWIP + →WIPG − → PRR
MLT + → DWIP + → WIPG − → PRR + → WIPI
Closed Loop
VUD − → UV + → UVD + → UDV or VUD − → UV+ → VCR+ → CV
Collection
CC + → VCR + →CV
CV + → VRFR − → CV
CV + → VAR − → CV
FP − → VAR
FP + → VRFR
Remanufacturing
VRFR +→ DV
VAR + → RV + → CVD
VAR + → RV +→ VRR + → ERR + → RR
Transshipment
DVO + → VSOR + → AIL + → AI + → VTR + → VC
MDBV + → TLT + → VUD −→ VTR +→ VC
MDBV + → VTR
AFR+→ AR
Vehicle Capacity
VC + → NAV − → VUT + → NAV
DNV + → VC and ACV + → VC

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