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A decision support framework for optimal vaccine distribution across a multi-tier cold chain network

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ABSTRACT

In this paper, we present a decision support framework for optimizing multiple aspects of vaccine distribution across a multi-tier cold chain network. We propose two multi-period optimization formulations within this framework: first to minimize inventory, ordering, transportation, personnel and shortage costs associated with a single vaccine; the second for the case when multiple vaccines with differing efficacies and costs are available for the same disease. We use the case of the Indian state of Bihar and COVID-19 vaccines to illustrate the implementation of the framework. We present computational experiments including what-if scenario and sensitivity analyses to demonstrate: (a) the organization of the model outputs; (b) how the models can be used to assess the impact of cold chain point storage capacities, transportation vehicle capacities, and manufacturer capacities on the optimal vaccine distribution pattern; and (c) the impact of vaccine efficacies and associated costs such as ordering and transportation costs on the vaccine selection decision informed by the model. We then demonstrate how robust optimization versions of the single vaccine model, with box and budgeted uncertainty sets, outperform the deterministic version under multiple levels of uncertainty in key model parameters. Finally, we also consider the computational expense of the framework for realistic problem instances, and suggest multiple preprocessing techniques to reduce computational runtimes. Our study presents a decision support framework that facilitates optimal distribution of vaccines from the manufacturer to the point of administration across a multi-tier vaccine cold chain network.

1. Introduction

The COVID-19 pandemic that originated in China rapidly spread throughout the world, and has caused more than five million deaths worldwide (Worldometers.info, 2022) and an estimated economic loss of nearly four trillion US dollars (statista.com, 2021). While moderately effective treatments have been developed, vaccines offer the best chance for a long-term solution to the pandemic. Therefore, a number of vaccines have been successfully developed and vaccination programmes across the world are being operationalized, with multiple large countries having vaccinated more than half their populations (World Health Organization, 2021). Successfully conducting a vaccination programme for a large population entails significant operational challenges (Azadi, Eksioglu, & Geismar, 2020; National Cold Chain and Vaccine Management Resource Centre, 2014). In particular, ensuring efficient distribution of the vaccines from the manufacturer to the medical centers where they are administered to eligible recipients among the public involves logistical challenges across multiple fronts. The challenge gets compounded especially when multiple tiers of the vaccine storage and distribution network need to be traversed. In this context, we present an integer linear programming based decision support framework that facilitates optimal distribution of vaccines from the manufacturer to the point of administration across a multi-tier vaccine cold chain network. We demonstrate the applicability of this decision support framework for the case of the distribution of COVID-19 vaccines across the state of Bihar in India.

In most countries, vaccines are typically ordered from their manufacturer by a central planning authority such as the central or state government. The vaccines are then routed through one or more storage/distribution facilities before they are delivered to the point of administration, typically a medical center such as a primary health center. Each of these storage/distribution facilities are referred to as a cold chain point, because majority of the vaccines must be stored...
and transported in refrigerated or sub-zero conditions. For example, in India, the vaccine cold chain of the public health system has multiple tiers: large government medical store depots (GMSDs) maintained by the central government, state level state vaccine stores (SVSs), regional vaccine stores (RVSs), and district vaccine stores (DVSs). The vaccines themselves are typically administered at medical facilities within a district which can be subcenters, primary health centers, community health centers, or district hospitals (National Cold Chain and Vaccine Management Resource Centre, 2014). Such multi-tier cold chains can be found in many countries. For example, Bangladesh has a four-tier vaccine chain: central vaccine store, district vaccine stores, Upazilla or subdistrict vaccine stores, with vaccines being administered at the next tier (unions and wards) (Guichard et al., 2010). Niger also has a four-tier vaccine cold chain similar to that of Bangladesh (Assi et al., 2013). The Indian multi-tier vaccine cold chain is depicted in Fig. 1. Given the multiple tiers of the vaccine supply chain and the associated complexities, the cost of the vaccine distribution process can be enormous unless it is optimized. While there are studies that optimize specific aspects of the vaccine distribution system, decision-makers will benefit from optimizing all aspects of the vaccine distribution process instead of specific components alone. Thus, it is evident that a comprehensive decision support framework for optimizing vaccine distribution across a multi-tier cold chain network can prove useful for health planning authorities. This forms the focus of this work.

We present in this paper a decision support framework, based on integer linear program (ILP) models, for optimal distribution of vaccines across a multi-tier cold chain network. The framework will enable decision-makers, such as public health planning authorities, to make the following decisions. Given a planning horizon of, say, $n$ weeks with projected vaccine demand for each population subgroup in each week, the framework will support optimal decision-making for deciding:

- Which manufacturer(s) the vaccines may be procured from, and the amount of each vaccine to procure – in each time unit – when multiple vaccines are available for a given disease;
- Whether a given facility in the cold chain must place an order in a given time unit, and if so, from which next higher-tier facility (when many options are available);
- Quantities of each vaccine (from a set of multiple vaccines available for a given disease) to be ordered at each cold chain tier at each time unit;
- Number of vehicles required to transport the vaccine quantities ordered – for each facility in the cold chain – at each time unit;
- The level of inventory to be maintained at each cold chain facility in the network at each time unit;
- Which vaccine to administer to each subgroup in each facility in a given time unit;
- The number of vaccination staff required in each facility in each time unit.

In addition to the above, the framework also allows analysts to perform various what-if scenario and sensitivity analyses to determine the impact of key logistical situations – such as the impact of variations in the production capacity of the vaccine manufacturer, efficiency of the vaccine ordering and transportation processes in each cold chain tier, and cold chain capacity – on the optimal ordering and inventory patterns for the planning horizon. The models in the proposed decision support framework attempt to optimize the above decisions by minimizing a total vaccine distribution cost that takes into account fixed and variable costs (where applicable) associated with each of the above decisions. For example, we consider fixed and variable ordering costs, inventory holding costs, and vaccination workforce resizing costs. Transportation costs considered in the model also include vehicle booking/mobilization as well as distance-based costs. We also incorporate measures that represent the level of vulnerability (and therefore, the priority) of each vaccine recipient subgroup by incorporating a shortage cost per recipient in each subgroup: higher the shortage cost, higher the vulnerability and therefore higher the priority of recipients in that subgroup. Vaccine costs and efficacies are also considered, facilitating decisions regarding which vaccine to order for a given disease.

The need to study the logistics of vaccine cold chain networks, especially during epidemics, has been established previously (Dasaklis, Pappis, & Rachaniotis, 2012). Previous work involving optimization of vaccine distribution has focused on three main areas. The first involves optimizing timing of vaccine development, and determining optimal vial size and vaccine inventory replenishment schedules (Azadi et al., 2020; Azadi, Gangamanavar, & Eksigolu, 2019). The second involves optimizing vaccine allocation across multiple recipient subgroups or geographical regions to minimize the impact of a disease (Yarmand, Ivy, Denton, & Lloyd, 2014). The third area involves optimizing aspects of production and distribution of vaccines (Hovav & Tsadikovich, 2015; Manupati et al., 2021). Our work is concerned with the third area, and our research contributions with respect to previous work in this area are detailed in the subsequent section. Overall, the lack of proper planning and scheduling of vaccine distribution in a vaccine supply chain, especially during the COVID-19 pandemic, has been highlighted by multiple experts as a key challenge, and our work attempts to address this challenge (Alam et al., 2021).

The rest of the paper is organized as follows. In the following section, we present the relevant literature and our research contributions. In Section 3, we describe the vaccine distribution problem, and the single-vaccine and multiple vaccine integer programming formulations. In Section 4, we illustrate the application of the single vaccine and multi-vaccine formulations for the COVID-19 case, and describe multiple what-if scenario and sensitivity analyses conducted using both formulations. In an electronic component accompanying this article, we also present robust optimization versions of the single vaccine model and potential methods to accelerate solution times for the models within the framework. In Section 5, we conclude the paper.

2. Literature review

In the vaccine supply chain literature, researchers have focused on the following main research directions: (a) vaccine composition, (b) allocation of vaccines among the target population, and (c) production and distribution of vaccines. Given the significantly more direct relevance of the third area, we discuss it below. We then provide an account of the literature on handling parameter uncertainty associated with vaccine supply chain models, and conclude with a listing of our research contributions with respect to the relevant literature.

2.1. Production and distribution of vaccines

Vaccine production is characterized by uncertain production yields and demand, longer manufacturing times and frequent changes in composition of vaccines. Federgruen and Yang (2008) study a problem in which the decision maker has to satisfy uncertain demand by sourcing vaccines from multiple suppliers who in turn have uncertain production yields. One way to manage uncertainty in production yields and demands is to adjust the pricing and selling strategies. Cho and Tang (2013) studied three selling strategies namely, advance, regular and dynamic selling. The authors analyze and present options that are beneficial to the manufacturer and the retailer. Eskandarzadeh, Eshghi, and Bahramgiri (2016) extended the work for a risk averse supplier in which the low production yield risk is controlled through pricing and quantity as decision variables. With regard to vaccine inventory management at a single site (e.g., a clinic), Lim, Norman, and Rajgopal (2017) develop a lean-inspired set of processes using secondary vaccine packaging and simplified inventory tracking for more efficient inventory management at the site under consideration.

With regard to vaccine distribution across a network of demand sites, Chen et al. (2014) develop a linear programming model for maximizing the number of fully immunized children. The authors assume...
that vaccine supply is sufficient to meet demand, consider costs to a very limited extent in their model, and also do not support decision-making regarding transportation or vaccination staff capacity as part of their model. In more recent work, Lim, Norman, and Rajgopal (2022) attempt to optimally redesign vaccine distribution networks entirely - that is, they optimize both the number of intermediate distribution centers (aside from the central store and vaccine administration clinics) and their location via a mixed integer formulation. They also determine the number of trips between tiers in their network required to fully meet vaccine demand. The authors motivate their work based on the study by Assi et al. (2013), who found via simulation that removing one of the intermediate tiers (the regional tier) of Niger’s vaccine cold chain improves the efficiency of vaccine distribution in achieving immunization coverage. This work builds on similar attempts by Yang (2020), Yang, Bidkhori, and Rajgopal (2021) that focus on the redesign of the vaccine distribution network of the World Health Organization’s Expanded Programme on Immunization. Another related work by Yang and Rajgopal (2021) considers optimizing immunization outreach activities in LMICs via a multiperiod ILP and stochastic modeling approach that accounts for uncertainties in accessibility of the target population.

We also discuss here the findings of a relatively recent review paper regarding vaccine supply chains. De Boeck, Decouttere, and Vandaele (2020) review the literature pertaining to vaccine distribution chains, including but not limited to the operations literature, on vaccine distribution chains in low- and middle-income countries (LMICs). The authors find that vaccine distribution planning across such cold chains must take into account storage, transportation as well as healthcare personnel capacity, and not focus on a subset of these resource categories alone. Among other findings, the authors also note the lack of literature that addresses allocation decisions to vulnerable subgroups when vaccine supply is limited. Further, the authors also comment on lack of data availability and reliability of available data pertaining to operational decisions in LMICs, such as inventory capacity, holding costs, and even vaccine demand. These findings are partially supported by another previously published review by Duijzer, van Jaarsveld, and Dekker (2018). We attempt to address these gaps via our proposed framework, which includes robust ILP models to account for uncertainty in operational data used to parameterize such models.

A key study relevant to our work – which is to develop a comprehensive framework for optimal vaccine distribution across an existing multi-tier vaccine cold chain network – is that by Hovav and Tsadikovich (2015). The authors present a multi-echelon (cost-benefit) model for inventory management of an influenza vaccine supply chain in Israel. The objective of the model is to minimize vaccination costs. The authors present a network flow approach to model the distribution of vaccines across their three-tier supply chain (manufacturers, distribution centers and recipients). The authors formulate the problem as a mixed-integer nonlinear optimization problem. In addition to the nonlinearity of their model, another main drawback of this study is that it does not consider the one-time distance-independent vehicle mobilization costs associated with transportation (e.g., the cost of booking a vehicle for transporting vaccines from one cold chain tier to another cold chain tier), and vaccination staffing decisions (they assume a fixed vaccination staff size). Our work addresses these shortcomings.

A recent study by Manupati et al. (2021) is also relevant to our work. The authors attempt to redesign the vaccine cold chain network, along with a decision support system based on decision-tree analysis and the synthetic control method for determining the allocation of vaccines to geographical regions and recipient subgroups. Once the allocation is determined, the authors formulate a mixed-integer linear program (which they solve via a heuristic) to determine the locations of intermediate cold storage facilities between the vaccine production facilities and the health centres.

2.2. Uncertainty modeling in supply chain applications

As outlined in the previous sections, the vaccine supply chain is inherently complex with uncertainties in product selection, production and distribution phases. At the selection stage, uncertainty arises when a public health organization (typically WHO) decides which variant of the virus should be targeted in the current vaccination season. Since vaccine production incurs a long lead time, manufacturers are typically unable to fully satisfy the demand in the vaccination season. The next level of uncertainty occurs in the yield of the production process at the manufacturer. The final level of uncertainty occurs in the demand side — for example, vaccine hesitancy in the target population, antigenic drift in the virus, etc. Researchers have primarily studied supply chain contracts as ways to deal with uncertainties arising in these scenarios. Cho (2010) studied the impact of yield uncertainty in an influenza vaccine supply chain in an uncertain product scenario — that is, uncertainty associated with which viral strain might cause an outbreak in the current season. The author proposes an optimal dynamic policy to improve social welfare. Cho and Tang (2013) studied three strategies to mitigate supply side and demand side uncertainty. The first is an advanced selling strategy where selling happens before both supply and demand is realized, the second involves regular selling where selling happens after the demand and supply are realized, and finally, the case of dynamic selling which incorporates both advanced and regular selling strategies. Arifoglu, Deo, and Irvani (2012) studied the impact of yield uncertainty and demand side uncertainty due to self-interested individuals on an influenza vaccine supply chain. Dai, Cho, and Zhang (2016) proposed supply chain contracts as a mechanism to address the problem of inefficiencies occurring due to supply side and demand side uncertainties. In recent work, Arifoglu and Tang (2021) propose vaccination incentives to the demand side and a “menu of transfer payments” to the supply side to mitigate inefficiencies occurring due to uncertainties in the influenza vaccination supply chain. Chandra and Vipin (2021) studied subsidy contracts to coordinate a vaccination supply chain with stochastic production yields. The authors show that subsidy contracts can achieve channel coordination in a vaccination supply chain with varying production yields.

Very few studies have used mathematical optimization techniques to deal with uncertainties arising in the vaccination supply chain. Ozaltun, Prokopyev, and Schaefer (2018) studied the composition and production decisions of influenza vaccine as a bilevel multi stage stochastic mixed integer program. At the upper level of the optimization problem, composition decisions (which influenza strains to include in the vaccine) are made while at the second level production decisions are made conditional to the upper level decisions. Sazvar, Tafakkori, Oladzad, and Nayeri (2021) studied a capacity planning problem in designing a resilient supply chain which faces uncertainties due to disruptions. The authors propose a multi-objective optimization model for the same. The authors incorporate redundant capacities as a means to counter risk arising from disruption.

In this work, we consider uncertainties in production and distribution by considering uncertainty in multiple parameters associated with vaccine distribution across the cold chain, such as vaccine ordering costs and holding costs, which are known to be difficult to estimate accurately (Hopp & Spearman, 2011). We consider two approaches to handling the uncertainty associated with key model parameters. First, we conduct comprehensive what-if scenario and sensitivity analyses associated with uncertainty in key model parameters such as storage and transportation capacity, manufacturing capacity, ordering costs, vaccine purchase costs (in the multiple vaccine case). This approach helps establish thresholds for each key parameter that, when breached, yields significant changes in vaccine inventory and distribution patterns across the cold chain. Secondly, we adopt a robust optimization approach to model the multi-echelon vaccine supply chain problem, and consider box and budgeted uncertainty sets for key model parameters.

In the following subsection, we present the main contributions of our study with respect to the extant literature.
2.3. Contributions of our study

The main contributions of our work with respect to the literature discussed above are listed below.

1. To the best of our knowledge, our model represents the most comprehensive multi-echelon inventory flow optimization model for a vaccine cold chain in terms of the set of decisions – facility selection at each tier, vaccine choice, vaccine quantities, number of transportation vehicles per time period, vaccination staff, recipient subgroups to be vaccinated, etc. – supported. This comprehensive modeling approach is adopted based on vaccine planning insights from De Boeck et al. (2020), and based on the lack of such comprehensive models in the Indian context. We note here that our approach does not involve redesigning the vaccine cold chain network, in contrast to the work by Manupati et al. (2021).

2. Our model is an integer linear program model of the network flow in a vaccine cold chain which, in contrast to the existing nonlinear integer program models developed for similar vaccine cold chain networks (Hovav & Tsadikovich, 2015), can yield exact optimal solutions. Further, the linear nature of such a comprehensive model also facilitates the development of pre-processing techniques for our formulations to help find optimal solutions within reasonable computational runtimes. This is demonstrated for the single vaccine model in this study.

3. To the best of our knowledge, our model provides the most comprehensive accounting of vaccine recipient subgroup prioritization considerations to date, and integrates the prioritization decision with regard to vulnerable subgroups within a single model, in contrast to the work by Manupati et al. (2021). Moreover, we extend our vaccine recipient subgroup prioritization ‘submodel’ to the case when multiple vaccines are available for the same disease, thereby providing decision support for which vaccine to administer to a given subgroup. We then illustrate via sensitivity analyses how the interplay between vaccine efficacies, their unit costs and logistical costs as well as subgroup vulnerability to the disease in question (quantified by subgroup-specific shortage costs) influences the decision of which vaccine to administer to which subgroup.

4. In our knowledge, our study is the first to provide a comprehensive approach towards considering uncertainty associated with vaccine distribution across cold chain networks both via comprehensive what-if scenario and sensitivity analyses involving key model parameters as well as by developing robust optimization versions of the single vaccine model.

Our model can be extended to any vaccine or even multiple vaccines together taking into account the respective capacity requirements of each vaccine. We deal with the tactical decisions of allocation-location as well as strategic decisions of capacity planning, inventory level management, and vaccine recipient subgroup choice.

3. Development of the decision support framework

In this section, we first describe the decision problem that our framework addresses, and then describe the mathematical models within our framework. We then outline the model parameter estimation process to conclude this section.

3.1. Decision problem description

We develop an integer linear programming based framework for optimizing the decisions that need to be taken with regard to vaccine distribution across a hierarchical cold chain network. We consider decisions associated with the logistics of ordering, transporting, storing, and administering vaccine doses across the cold chain network. In addition to the above set of logistical decisions that are key to any supply chain network, we also introduce vaccination staff capacity planning at the last tier of the cold chain as the number of vaccine units that can be administered at any health centre would depend on the availability of the health workers responsible for doing so. We also consider decisions regarding the prioritization of vulnerable subgroups of eligible recipients of vaccine units within our framework by associateing subgroup-specific unit costs of not vaccinating a recipient belonging to each subgroup. We illustrate this by categorizing potential recipients by age. We consider this particular criterion for subgroup formation given its wide use in COVID-19 vaccination policies across the world. For example, during the COVID-19 pandemic, elderly patients were the first group in India, after healthcare workers, to be administered the vaccine on account of the higher case fatality rates among this age group (Bagcchi, 2021). Further, a similar classification of the recipient population was also used by Hovav and Tsadikovich (2015) for the case of influenza vaccination.

Decision-making in our framework starts from when the vaccines are ready to be transported from the manufacturer(s) through the subsequent tiers at different time periods. We associate one or more costs with every decision that we consider in our model, and hence the models within our framework aim to minimize a stylized total cost of operating a vaccine cold chain subject to cold chain storage capacity, transportation capacity, vaccination staff capacity, and administrative constraints. Given that we illustrate the application of our framework to the cold chain network in India, we now provide a brief overview of the same.

In India, the vaccine cold chain consists of the following tiers after the manufacturer, listed from the highest tier onwards to the lowest tier: GMSD (Government Medical Store Depot), SVS (State Vaccine Store), RVS (Regional Vaccine Store), DVS (District Vaccine Store) and the clinics (PHCs, CHCs and DHs) where the vaccines are actually administered to the intended recipients. The schematic of the flow of vaccines through the cold chain is shown in Fig. 1.

India has 7 GMSDs located mostly in major cities: Mumbai, New Delhi, Chennai, Kolkata, Hyderabad, Guwahati and Karnal. It has 39 state vaccine stores, 123 regional vaccine stores, 644 district vaccine stores, and 20000+ public health centres (which include primary and secondary care facilities) spread across the country (Inclentrust, 2011). For our analysis, we consider the Indian state of Bihar, which has one state vaccine store (SVS) located at its capital city, Patna. We construct a framework that encompasses all the cold chain tiers in Fig. 1; however, our framework can be utilized even if, in practice, one or more tiers do not play a role in a given region in vaccine distribution. From a modeling standpoint, we assume that vaccine manufacturers ship vaccine doses to the GMSDs, which in turn ship to the SVS in the state under consideration. These supply vaccines to the entire state through intermediate levels or tiers comprising of regional vaccine stores (RVS) and district vaccine stores (DVS). DVSs then transport the vaccines to primary health centres (PHCs) and community health centres (CHCs) which actually administer the vaccine doses to the local population.

In the total operating cost of the cold chain we include vaccine inventory ordering and holding costs at each CCP, one-time vehicle mobilization costs that are incurred irrespective of the distance between cold-chain facilities, and distance-dependent transportation costs that depend on the distance between CCPs and include fuel, costs of maintaining cold storage in the vehicles, etc. As mentioned earlier, we also include the cost of vaccines, and shortage costs associated with not vaccinating an eligible recipient which are different for different population subgroups, depending upon the extent of vulnerability of each subgroup. We also consider wages, hiring and firing costs of health workers to facilitate vaccination staff capacity planning. We describe how these parameters were estimated later in this section.

We develop integer linear programs that consider a single vaccine for a given disease as well as multiple vaccines for a disease. We begin by describing the single vaccine formulation.
3.2. Single vaccine model

We list below all the index sets associated with the single vaccine model, including index sets for each cold chain tier, recipient subgroups and time periods.

- Manufacturer index, $m \in \{1, 2, \ldots, M\}$
- Government medical store depot index, $g \in \{1, 2, 3, \ldots, G\}$
- State vaccine store index, $s \in \{1, 2, 3, \ldots, S\}$
- Regional vaccine store index, $r \in \{1, 2, 3, \ldots, R\}$
- District vaccine store index, $d \in \{1, 2, 3, \ldots, D\}$
- Primary health center index, $i \in \{1, 2, 3, \ldots, I\}$
- Recipient subgroup index, $j \in \{1, 2, 3, \ldots, J\}$
- Time period index, $t \in \{1, 2, 3, \ldots, T\}$

### Model parameters

- Inventory holding cost parameters at each cold chain point: $h^s_i$, $h^g_i$, $h^d_i$, $h^t_i$. Units: INR/dose/week.
- Transportation cost per vehicle transporting vaccines from one cold chain point to another cold chain point at the next tier (e.g., manufacturer $m$ to GMSD $g$, or DVS $d$ to clinic $i$): $K^{mg}$, $K^{gs}$, $K^{rs}$, $K^{td}$. Units: INR/truck.
- Transportation cost = (distance-dependent costs [diesel costs + labour costs + refrigeration costs] + one-time vehicle mobilization cost) × number of vehicles.
- Vaccine inventory holding capacity at each CCP: $B^s_i$, $B^g_i$, $B^d_i$, $B^t_i$. Units: doses.
- Capacity of each vehicle transporting vaccines from one CCP to the next lower-tier CCP (e.g., manufacturer $m$ to GMSD $g$, or DVS $d$ to clinic $i$): $C^{mg}$, $C^{gs}$, $C^{rs}$, $C^{td}$. Units: doses/vehicle.
- Fixed cost (ordering) of ordering vaccine by a CCP at a given level from the next higher-tier CCP (e.g., GMSD $g$ from manufacturer $m$, or clinic $i$ from DVS $d$): $S^{mg}$, $S^{gs}$, $S^{rs}$, $S^{td}$. Units: INR/order.
- Maximum number of vehicles available for transportation from one CCP to the next lower-tier CCP (e.g., manufacturer $m$ to GMSD $g$, or DVS $d$ to clinic $i$): $N^{mg}$, $N^{gs}$, $N^{rs}$, $N^{td}$. Units: vehicles/week.
- Lead times of delivery of vaccines from one CCP to the next lower-tier CCP (e.g., manufacturer $m$ to GMSD $g$, or DVS $d$ to clinic $i$): $L^{mg}$, $L^{gs}$, $L^{rs}$, $L^{td}$. Units: weeks.
- Lead times of administration of vaccines to subgroup $j$ at the clinics ($i$): $L^j_i$. Units: weeks.
- Initial inventory held at the CCPs: $I^0_s$, $I^0_g$, $I^0_d$, $I^0_t$. Units: doses.

### Miscellaneous parameters:

- Demand by subgroup $j$ at clinic $i$ at time $t$ (in doses/week): $D^j_i$
- Shortage cost (INR) of not vaccinating a customer in subgroup $j$ at time $t$: $P^j_i$
- Clinical services cost per customer in subgroup $j$ (e.g., INR/dose): $C^j_i$
- Average time (e.g., minutes/dose) required for administration of one vaccine dose: $T_o$
- Availability of a health worker in hours at clinic $i$ for time period $t$ (e.g., 40 h/week): $N^h_i$
- Production capacity of manufacturer $m$ at time $t$ (in doses): $B^m_i$
- Wastage factor (proportion of each dose wasted; i.e., effective dose volume required per dose is $\frac{1}{w}$): $w$
- Wages of health workers per time period (e.g., INR/week): $L$
- Fixed cost (INR) of hiring one health worker: $E$
- Fixed cost (INR) of firing one health worker: $F$
- Probability of exposure to the disease-causing pathogen: $p$
- Probability of not developing the disease after vaccination upon exposure to the pathogen (i.e., vaccine effectiveness): $\eta$

#### Total Demand

The following is the total demand by all the subgroups at all the clinics across the entire planning horizon.

$$Q = \sum_{t=0}^{T} \sum_{i=1}^{I} \sum_{j=1}^{J} \frac{D^j_i}{w}$$

### Decision Variables

- Number of vaccine doses held at each CCP at the end of time $t$ (non-negative integer): $I^t_s$, $I^t_g$, $I^t_d$, $I^t_t$.
- Number of vaccine doses delivered from one CCP to the next lower-tier CCP at the beginning of time $t$ - for example, from manufacturer $m$ to GMSD $g$, or from DVS $d$ to clinic $i$ (non-negative integer): $q^{mg}_t$, $q^{gs}_t$, $q^{rs}_t$, $q^{td}_t$.
- Number of vehicles required for transporting vaccines from one CCP to the next lower-tier CCP at time $t$ - for example, from manufacturer $m$ to GMSD $g$ (non-negative integer): $n^{mg}_t$, $n^{gs}_t$, $n^{rs}_t$, $n^{td}_t$. 
– Binary assignment variable indicating whether an order has been placed from a CCP by the next lower-tier CCP (e.g., order placed by GMSD \( g \) from manufacturer \( m \)): \( x_{m, g, t}^{mg} \), \( x_{s, t}^{st} \), \( x_{r, t}^{rt} \), \( x_{d, t}^{dt} \), \( x_{i, t}^{it} \)

– Number of persons not vaccinated (i.e., number of shortages) and number of vaccine doses administered in subgroup \( j \) in clinic \( i \) at time \( t \), respectively (non-negative integer): \( u_{j, i, t} \), \( s_{j, i, t} \)

– Number of health workers working, hired and fired in clinic \( i \) at time \( t \) respectively (non-negative integer): \( n_{j, i, t} \), \( h_{j, i, t} \), \( f_{j, i, t} \)

### Objective Function

\[ \text{Min } J_{\text{HCO}} = \]

\[ \sum_{m=1}^{M} \sum_{g=1}^{G} q_{m, g, t}^{mg} + \sum_{s=1}^{S} \sum_{t=1}^{T} q_{s, t}^{st} + \sum_{r=1}^{R} \sum_{t=1}^{T} q_{r, t}^{rt} + \sum_{d=1}^{D} \sum_{t=1}^{T} q_{d, t}^{dt} + \]

\[ \sum_{i=1}^{I} \sum_{j=1}^{J} s_{j, i, t}^{si} + \sum_{j=1}^{J} \sum_{i=1}^{I} u_{j, i, t}^{ui} + \sum_{i=1}^{I} \sum_{j=1}^{J} \eta_{j, i, t}^{\eta} \]

\[ \text{subject to: } \]

\[ \sum_{g=1}^{G} q_{m, g, t}^{mg} \leq B_{m}^{n} \forall m, t \]  \hspace{1cm} (1)

\[ \sum_{s=1}^{S} x_{s, t}^{st} \leq 1 \forall s, t \]  \hspace{1cm} (2)

\[ \sum_{r=1}^{R} x_{r, t}^{rt} \leq 1 \forall r, t \]  \hspace{1cm} (3)

\[ \sum_{d=1}^{D} x_{d, t}^{dt} \leq 1 \forall d, t \]  \hspace{1cm} (4)

\[ q_{m, g, t}^{mg} \leq (N^{mg}C_{t}^{mg}) x_{m, g, t}^{mg} \forall m, g, t \]

\[ q_{s, t}^{st} \leq (N^{st}C_{t}^{st}) x_{s, t}^{st} \forall g, s, t \]

\[ q_{r, t}^{rt} \leq (N^{rt}C_{t}^{rt}) x_{r, t}^{rt} \forall s, r, t \]

\[ q_{d, t}^{dt} \leq (N^{dt}C_{t}^{dt}) x_{d, t}^{dt} \forall r, d, t \]

\[ q_{i, t}^{it} \leq (N^{it}C_{t}^{it}) x_{i, t}^{it} \forall d, i, t \]

\[ \frac{q_{m, g, t}^{mg}}{C_{t}^{mg}} \leq n_{m, g}^{m} \forall m, g, t \]

\[ \frac{q_{s, t}^{st}}{C_{t}^{st}} \leq n_{s, t}^{s} \forall g, s, t \]

\[ \frac{q_{r, t}^{rt}}{C_{t}^{rt}} \leq n_{r, t}^{r} \forall s, r, t \]

\[ \frac{q_{d, t}^{dt}}{C_{t}^{dt}} \leq n_{d, t}^{d} \forall r, d, t \]

\[ \frac{q_{i, t}^{it}}{C_{t}^{it}} \leq n_{i, t}^{i} \forall d, i, t \]

In our proposed multiple vaccine formulation, the cold chain points are indicated by the same indices as for the single vaccine formulation. However, we have an additional index for the vaccine type.

- Vaccine index, \( k \in \{1, 2, 3, \ldots, K\} (K \leq M) \)

In the below specification of the formulation for the multiple vaccine case, we only provide the parameters, decision variables and constraints that change between the single and multiple vaccine formulations.

### 3.3. Multiple vaccine model
Parameters

– Inventory holding costs for vaccine k at each cold chain point: $h^{k}_{l}$, $h^{k}_{t}$, $h^{k}_{d}$, $h^{k}_{i}$. Units: INR/dose/week.
– Fixed cost (ordering) of ordering vaccine by a CCP from the next higher-tier CCP (e.g., GSMD g from manufacturer m, or clinic i from DVS d): $S^{mg}_{k}$, $S^{ti}_{k}$, $S^{rd}_{k}$, $S^{ij}_{k}$. Units: INR/-delivery. Note that the parameters $S^{mg}_{k}$ alone are indexed by vaccine type (the index k) along with manufacturer, GSMD and time. This is done to account for the possibility that a manufacturer may supply more than one vaccine and the fact that different vaccines may have different ordering processes at the interface between the manufacturer and the government, and hence may incur different ordering costs.
– Initial inventory of vaccine k held at the CCPs: $I^{kg}_{0}$, $I^{ki}_{0}$, $I^{rd}_{0}$, $I^{ij}_{0}$. Units: doses.

Miscalibrated parameters:

– The production capacity of manufacturer m for vaccine k at time $t$ (in doses): $B^{mk}_{t}$
– Packed vaccine volume per dose (cm$^3$/dose) of vaccine k: $P_{k}$
– Probability of not developing the disease after vaccination by vaccine k upon exposure to SARS-CoV2: $\eta_{k}$

Decision Variables

– Number of doses of vaccine k held at each CCP at the end of time $t$ (non-negative integer): $I^{kg}_{t}$, $I^{ki}_{t}$, $I^{rd}_{t}$, $I^{ij}_{t}$
– Number of doses of vaccine k delivered from one CCP to the next lower-tier CCP at the beginning of time $t$ - for example, from DVS d to clinic i (non-negative integer): $q^{mg}_{ki}^{kg}_{t}$, $q^{ti}_{ki}^{ki}_{t}$, $q^{rd}_{ki}^{rd}_{t}$, $q^{ij}_{ki}^{ij}_{t}$

– Binary assignment variable indicating whether an order has been placed from a CCP by the next lower-tier CCP (e.g., order placed by GSMD g from manufacturer m): $x^{mg}_{t}$, $x^{ti}_{t}$, $x^{rd}_{t}$, $x^{ij}_{t}$. Note that, similar to the vaccine ordering costs, the decision variables $q^{mg}_{ki}^{kg}_{t}$ alone are indexed by vaccine type (the index k) along with manufacturer, GSMD and time indices.

Objective Function

\begin{align}
\text{Min } J = \sum_{k} \sum_{m} \sum_{d} K^{mk}_{d} h^{k}_{d} + \sum_{k} \sum_{i} \sum_{k} K^{ki} h^{k}_{i} + \sum_{k} \sum_{d} \sum_{r} K^{rd} h^{k}_{d} + \sum_{k} \sum_{i} \sum_{j} K^{ij} h^{k}_{i} + \sum_{k} \sum_{i} \sum_{j} \sum_{t} F \sum_{i} \left(1 - \eta_{i} \right) p_{i}^{t} u_{ij}^{t}.
\end{align}

The terms in each line of the objective function above represent the same types of costs as those in the objective function of the single vaccine formulation. The constraints below are largely self-explanatory given the context of the single vaccine model. Note that the facility selection and vaccination workforce balance constraints remain the same as for the single vaccine case, and hence are not provided in the set below.

Subject to constraints:

\begin{align}
\sum_{g} q^{mg}_{ki}^{kg} \leq B^{mk}_{t} \quad \forall \ k, m, t
\end{align}
also be defined in terms of the total volume available for storage of the vaccine(s) under consideration. The former approach (i.e., the dose-based capacity definition), which we have adopted in the formulations in our framework (including the multiple vaccine formulation) involves computing the total volume available for storage of the vaccine(s) under consideration and then dividing by the packed volume(s) per dose of the vaccine(s). The latter approach involves using the volume directly, which may be more convenient if the vaccines that use the transportation vehicle or CCP storage facilities differ widely in their packed volumes per dose.

The models in our framework can be modified easily to incorporate one or the other approach based on the preference of the analyst using the framework. For example, in the single vaccine model described above, if the volume-based approach for defining inventory capacity \( B^a_T \) is used (i.e., \( B^a_T \) is defined in terms of CCP volume available for the vaccine under consideration), and the inventory \( I^a_T \) stored at said CCP in time is continued to be defined in terms of doses, then constraint (6) becomes:

\[ I^a_T \leq \frac{1}{v} B^a_T \forall a, t \text{ where } a \in \{g, s, r, d, i\} \]

Here \( v \) represents the packed volume per dose of the vaccine. Note that if the vaccine is provided in the form of multi-dose vials, then further minor modifications may need to be made to the formulations.

We now describe how the parameters associated with our formulations are estimated.

### 3.4. Model parameter estimation

To illustrate the implementation of our framework, we work with the Indian state of Bihar. The vaccine delivery network in Bihar operates through 1 SVS, 9 RVSS, 38 DVSS, and 606 clinics (Ministry of Health and Family Welfare, 2017). The map of the cold chain network in Bihar is shown in Fig. 2.

**Estimation of cold chain and transportation vehicle capacity**

There are 654 cold chain points within the vaccine distribution network in the state of Bihar. Through our data collection process, we determined that a total of 1946 cold chain equipment – such as walk-in freezers, coolers, and ice-lined refrigerators – are used across the cold chain network in the state (Ministry of Health and Family Welfare, 2017). The numbers of each equipment type, the dimensions of the refrigerated and insulated vans (National Cold Chain and Vaccine Management Resource Centre, 2014) and the cold boxes (Ministry of Health and Family Welfare, 2016) and estimates of other associated parameters such as the utilization factor are given in Table A.3 in Appendix A. We have assumed that the cold chain equipment for a given district is uniformly distributed across all its health centers where the vaccines are administered. For calculating the capacity of these cold chain equipment, the packed vaccine volumes per dose for the two types of COVID-19 vaccines were taken from official data released by the Indian government (Ministry of Health and Family Welfare, 2021).

Vaccines are transported in refrigerated vans from the manufacturer to the GMSD and from the GMSD to the SVS (for long distances), and in insulated vans from the SVS to all other downstream cold chain points (National Cold Chain and Vaccine Management Resource Centre, 2014). The capacities of these vans were calculated by assuming standard dimensions of the vehicles with a certain utilization factor. Utilization factor is assumed to be a number less than 1 that is multiplied with the storage shelf volume to arrive at the actual fraction of space available for storing vaccines. This is due to the fact that the entire storage space available for storing vaccines cannot be used due to loss of vaccine doses caused by vaccine handling practices, packaging dimensions, etc. The most commonly used estimate for this parameter is 0.67 (World Health Organization, 2017). The distances between each CCP were estimated via the Bing Maps application, and used to populate a distance matrix. The distance is then multiplied by fuel (diesel) cost to get the distance-dependent transportation cost. One-time vehicle mobilization costs have been estimated from commonly used vehicle-booking services in the Indian context.

**Estimation of demand**

In order to demonstrate how the optimization framework can be used to prioritize certain subpopulations over others, we assumed that
the population of the state can be divided into three subgroups categorized on the basis of age: children (less than 18 years), adults (between 18 to 60 years) and elderly (60 years and above). Assuming one dose of vaccine administered per person within a given planning horizon, the weekly demand for each subgroup at each clinic is calculated from the population distribution by age among all the districts in the state. The population distribution by age was obtained from the most recent census data published by the Indian government (Ministry of Health Affairs, 2011a). This is multiplied with the growth rates by age group (Ministry of Health Affairs, 2011b) to arrive at the estimates of the population size of each subgroup.

Estimation of other parameters

The production capacity of the manufacturer has been assumed to be around 2 billion doses for the entire country (European Pharmaceuticals, 2020). However, as shown in Section 4.1, we analyze how the manufacturing capacity affects the extent to which demand is satisfied across the planning horizon.

The inventory holding cost has been assumed to be Rs 0.3 per unit vaccine per week for all CCPs at all the tiers. The ordering costs at each tier have been reasonably assumed with costs per order increasing with the level of the CCP tier. We note here that the vaccine ordering costs at each cold chain tier can be considered to be proxy measures of the efficiency of the ordering process at a given tier. Thus these costs can be adjusted depending upon the perception of the decision-maker or analyst using this proposed decision support tool regarding the efficiency of the ordering process at a given cold chain tier. Note that ordering costs can be varied across specific facilities within a cold chain tier. Hence it is the relative values of the ordering costs both within and across cold chain tiers that are of more importance than the actual estimates themselves. A similar argument can be made for the one-time vehicle mobilization costs associated with transportation as well.

The wages, hiring, and firing cost of vaccination staff have been estimated by collecting data on standard wages. The wages are taken as the median salary of nurses (monthly) in Bihar which are adjusted appropriately to obtain the weekly wages. The hiring and firing costs have been accordingly assumed as some proportion of the monthly salary of the nurses.

We explain the estimation of the shortage costs within the context for the multiple vaccine model, which we can consider as a generalization of the single vaccine model. We develop our modeling of the costs of not vaccinating eligible recipients based on the notion of shortage costs introduced in Hovav and Tsadikovich (2015), who in turn base their shortage cost calculation model on the work by Clements, Chancellor, Nichol, DeLong, and Thompson (2011) and Molinari et al. (2007) for the influenza vaccine. Shortage costs in both Hovav and Tsadikovich (2015) as well as in our study are estimated based on the difference between the average cost of illness from an unvaccinated person and the average cost of illness from a vaccinated person. However, the exact shortage cost calculation model in our study is different from that used in Hovav and Tsadikovich (2015), given that we: (a) incorporate the multiple vaccine case, which involves including a measure of vaccine effectiveness in the shortage cost model, and (b) include the costs of the loss of life due to the disease in question, as well as the costs of illness (but not mortality), among both vaccinated and unvaccinated persons. The shortage costs are included in the objective function of the multi-vaccine formulation in the following manner:

\[
\sum_{t} \sum_{j} \sum_{k} \theta P_{ij}^{t} + \sum_{t} \sum_{i} \sum_{j} \sum_{k} (1 - \eta_{k}) P_{ij}^{t} c_{ij}^{t} k
\]

The above terms consider the cost of illness from COVID-19 among different subgroups, weighted by probability of exposure to the disease-causing pathogen and the effectiveness of the vaccine, for both unvaccinated (first term) and vaccinated persons (second term). Here \( p \) is the probability of exposure to the SARS-CoV2 virus (we assume exposure to the virus leads to developing symptomatic or asymptomatic COVID-19 with 100% probability), and \( \eta_{k} \) is the effectiveness of the vaccine in preventing symptomatic infection. Thus \( 1 - \eta_{k} \) represents the probability of developing COVID-19 upon exposure to the virus after getting vaccinated. The probability of exposure to the disease \( p \) can be estimated using serosurvey data (for example, 56% of the population residing in certain areas of New Delhi were found in a serosurvey to have COVID-19 antibodies (The Hindu, 2021) or can even be set to 1.0 for endemic diseases. We multiply both terms by \( P_{ij}^{t} \) (the cost of illness for a person in the \( j \)th subgroup developing a symptomatic form of the disease under question) to get the costs incurred in each case. We propose the following formula to estimate \( P_{ij}^{t} \):

\[
P_{ij}^{t} = [m_{i} (L - \bar{A}_{j}) + (1 - m_{i})] \times R
\]

Thus we consider two types of costs associated with illness from COVID-19. The first term captures indirect costs; that is, it quantifies the loss of productivity from mortality due to COVID-19, estimated by the per-capita income of the country in question. The second term captures the direct cost of illness incurred due to COVID-19 incurred by those who survive the illness. In the equation above, \( m_{i} \) is the case fatality rate for the disease for the \( j \)th subgroup, thereby capturing the vulnerability of the subgroup to the disease in question. In the above equation, \( I \) is the per-capita income, \( \bar{A}_{j} \) is the average age in the \( j \)th subgroup, \( L \) is the population average life expectancy and \( R \) is the cost of treatment incurred by the payer (e.g., the government, or the societal cost as a whole) per case of the disease. Vaccine effectiveness \( (\eta_{k}) \) values have been taken from the official data given for each vaccine. A serosurvey (which tested people for COVID-19 antibodies via serological tests) was conducted in Delhi in the month of January 2021, and estimated that about 56% of the Delhi residents were exposed to the SARS-CoV2 virus (The Hindu, 2021). This gives us an estimate of \( p \), the probability that a person is exposed to the virus. We considered the most recent estimate of the case fatality rate of COVID-19, found out the difference between the average age of the subgroup and life expectancy (~69 years) (World Bank, 2018) and multiplied this with the per capita income (INR 1,25,408) (Financial Express, 2019) of India to estimate the shortage cost in case the person dies from COVID-19. If the person does not die (the probability of survival is \( 1 - m_{i} \)), then additional treatment fees are incurred which is given by \( R \). These estimates were rounded to obtain the shortage costs actually used in the model. We would like to emphasize here that we provide these details to illustrate how shortage costs for a particular vaccine can be calculated and that this may be modified based on the disease under consideration as well as the data available for the vaccine(s) and the disease. For example, we assume that the mortality probability remains the same for vaccinated and unvaccinated people; however, this can be modified easily if required. Further, the shortage cost \( P_{ij}^{t} \) is allowed to change with the time period \( t \) in the planning horizon. This implies that particularly vulnerable subgroups – such as elderly patients with comorbidities – can be assigned substantially higher shortage costs at the beginning of the planning horizon so that their vaccination is prioritized above all other subgroups.

The fraction of available CCP and transportation vehicle storage capacity for COVID-19 vaccine has been estimated as a ratio of the total demand for COVID-19 to the total demand for all the other vaccines, taking into account their respective packed vaccine volumes per dose. We note here that a single average packed vaccine volume per dose is taken for all the other vaccines for ease of calculation.

The values for each of the estimated/assumed parameters are given in Table A.4.

We now discuss the computational implementation of the model framework, and illustrate its use to determine the impact of various logistical as well as vaccine-related considerations on the optimal distribution of vaccines across the cold chain network.

9
4. Decision support framework uses: Computational illustration

In this section, we provide a comprehensive demonstration of how the decision support framework can be used to not only generate optimal logistical plans for the distribution of vaccines across the cold chain network, but also conduct what-if scenario and sensitivity analyses associated with various logistical situations such as those of low CCP storage and transportation capacities and limited manufacturing capacity. In these analyses, we do not examine the impact of perturbing every single model parameter. Instead, we consider key parameters that are likely to have a significant impact on optimal vaccine distribution patterns given a certain constant recipient demand. These include storage and transportation capacities, manufacturing capacity, holding and ordering costs, and when multiple vaccines are involved, differences in efficacy and purchase costs. Further, we do not examine the optimal objective function value when these parameters are changed in our analyses because the objective function is a stylized quantity constructed to yield meaningful vaccine distribution patterns, and instead focus on changes in the vaccine distribution and inventory patterns across the cold chain.

We organize our presentation of the numerical experiments that we perform with the models in the framework as follows. In Section 4.1, we demonstrate the analyses that can be carried out using the single vaccine model. As part of this, in Section 4.1.1, we describe how the model's outputs can be organized and presented concisely, and explore the impact of changing vaccine transportation capacity and lead times on the optimal distribution of the vaccine across the cold chain. Following this, in Section 4.1.2, we examine in detail the impact of CCP storage and transportation capacities on vaccine shortage patterns among each population subgroup, and in Section 4.1.3, we study the impact of storage and transportation capacities on inventory patterns across the cold chain. In Section 4.1.4, we consider the impact of limiting vaccine manufacturing capacity, which was a significant concern during the COVID-19 pandemic, on optimal vaccine distribution patterns.

In Section 4.2, we consider the multiple vaccine model. First, in Section 4.2.1, we provide an overview of outputs from the multiple vaccine model, and discuss certain assumptions associated with modeling vaccine efficacy. Then, in Section 4.2.2, we discuss in detail the impact of multiple logistical and vaccine-related considerations – such as each vaccine's manufacturing capacity, vaccine efficacy, etc. – on the choice and quantity of each vaccine that is recommended for administration as part of the output of the multiple vaccine model.

Finally, in Section 1 of the electronic component accompanying this article, we discuss how the robust formulation can be used and its performance with respect to the standard single vaccine formulation. In Section 2 of the electronic component, we also consider the computational cost of the single vaccine formulation, and discuss preprocessing techniques that can be used to speed up solution generation as well as improve the quality of the solutions.

4.1. Single vaccine model

4.1.1. Overview of model outputs, impact of transportation capacity and lead times on optimal logistical patterns

We begin by demonstrating the output of the single vaccine model within the decision support framework that we develop. In order to illustrate how the output of the decision support framework can be organized and analyzed, we consider a relatively small component of the cold chain in the state of Bihar, especially at the district level: we include only two districts (which we refer to henceforth as districts 1 and 2, respectively). This implies that in addition to the manufacturer, the GMSD, the SVS, and 9 RVSs, we consider 2 DVSs and 16 clinics, with 10 located in district 1 and 6 in district 2. Further, for ease of representation of the model output, we consider a 6 week planning horizon.

We present the output of the single vaccine model for the above cold chain for two cases: in the first case, all model parameters are estimated from Table A.4 (which we refer to as the base case), and in the second case, we consider a vaccine with a higher packed volume per dose of 3.3 cm$^3$/dose (for the measles vaccine). We present the model output in this manner because the COVID-19 vaccine packed volumes per dose (e.g., 0.211 cm$^3$/dose) appear to be significantly lower than those of other commonly used vaccines, implying that the capacity required to transport and store vaccines other than the COVID-19 vaccines is likely to be significantly lower. This also provides us with an opportunity to demonstrate how storage and transportation capacity affects the optimal ordering, inventory storage, shortages, and staffing decisions associated with vaccine distribution across the cold chain. The output for the base case is provided in Table 1 and the output for the higher packed volume per dose case is provided in Table 2. Tables 1 and 2 do not list the decisions for every facility in the cold chain network; from the sake of brevity, they only contain the facilities between which vaccines are transported in a given time period. For example, for the base case, we see that all of the ordering and transportation occurs in week 1, and that the vaccines are transported to the clinics along the following path: manufacturer → the GMSD → the SVS → RVS 5 → DVS 1 → the clinics.

We first note from Tables 1 and 2 that the number of shortages incurred (Tables 1,2), the inventory held at different time periods across the planning horizon at different CCPs, which we refer to henceforth as the inventory pattern (Tables 1, 2) and the vaccination staff's recruitment schedule (Tables 1, 2) remain the same for both the cases. However, we see that the ordering and vaccine transportation patterns as seen in Tables 1 and 2 are different when the storage and transportation capacity are significantly different.

We observe that for the base case, a single DVS (DVS 1) supplies the vaccine units to all the 16 clinics. It receives the entire supply from a single RVS (RVS 5), which happens to be the nearest RVS to the SVS. The reason for a single cold chain point handling the entire supply in the RVS and DVS tiers is the higher capacity available for transportation due to lower packed volumes (more than 2.5 million doses per vehicle from both the district and the regional level). All the 16 clinics order from only district 1 because the shortest route, in terms of the sum of the distances of the clinics and RVSs from DVS 1 and DVS 2, is the lowest for RVS 5 and DVS 1 among all possible routes.

However, this does not hold for the case with the higher packed volume per dose. A single district cannot cater to the demand of all 16 clinics because of the reduced transportation capacity available for vaccines with higher packed volume per dose. A vehicle from a DVS can only transport 171,736 doses at a time, which is less than the combined demand of all the clinics (333,616 doses). Therefore, the supply gets split among the two districts, with both districts ordering their respective vaccine quantities from RVSs 5 and 6, which are the nearest RVSs to the SVS. Also, we notice that 'cross-ordering' from the DVSs occurs at the clinic level, which means that certain clinics receive vaccines from DVSs in districts other than the district in which they are located. This happens primarily because of the restriction on transportation capacity. If the clinics were to order from the DVSs in their district only, then additional orders would need to be placed, which in turn result in additional ordering and transportation costs. This does not occur given the overall cost minimization objective across the cold chain. This analysis thus illustrates the interplay of the ordering costs, transportation distances, and vaccine transport vehicle capacity. Therefore, the optimal ordering and vaccine transport pattern that our proposed framework yields does not necessarily conform to the 'shortest' paths (based on inter-facility distances) across the cold chain. Other factors, an example being the vaccine transport vehicle capacities, also play an important role in guiding the logistics of distribution and administration of vaccines.

We also notice from Tables 1 and 2 that there are shortages in weeks 1 and 2 in both the cases, which result in shortage costs being incurred.
In continuation with the above analyses, we study the impact of cold chain capacity in more detail – storage and transportation vehicle capacity – on the optimal shortage and inventory patterns generated by our model. For this, using the high packed volume per dose case (as packed volumes per dose higher than that of the COVID-19 vaccines appear to be more prevalent), we vary the fraction of the storage and transportation capacity available for the vaccine under consideration and report the total shortages incurred at the end of the planning horizon and the inventory pattern at each cold chain tier. We find that for a given parameterization of the model, there exists a threshold or critical value of this fraction (for example, 0.125 for the adult subgroup) above which the number of shortages incurred among a particular subgroup becomes constant. Below this fraction, the number of shortages increases and consequently result in increasing shortage costs as well. In addition to the decreased storage capacity, the cap on the number of vehicles that are available at a cold chain point for transportation to the next lower-tier cold chain point also leads to this increase in the number of shortages incurred. Further, the critical fraction of cold chain capacity below which the shortages start increasing remains the same regardless of the lead times assumed across the cold chain, as this increase in the shortages is only due to the limits on storage and transportation capacity and is not related to the lead time.

We also note that even at low capacities, the proportion of eligible recipients in each subgroup not receiving the vaccines is the lowest in the highest priority (or most vulnerable) subgroup (0% in elderly) and the highest in the lowest priority subgroup (close to 100%) at lower fractions of available capacity. In other words, the subgroup with a higher shortage cost (a proxy for higher vulnerability, and therefore, higher priority for vaccination) is always catered to first, after which other subgroups are considered. The above results are

| Route            | Week | Ordering pattern | Quantity | Transportation costs (INR) | Total | Ordering costs (INR) |
|------------------|------|------------------|----------|---------------------------|-------|----------------------|
| M → GMSD         | 1    | 333,616          | 40,000   | 14,000                    | 54,000| 200,000              |
| GMSD → SVS       | 1    | 333,616          | 20,000   | 7,700                     | 27,700| 100,000              |
| SVS → RVS 5      | 1    | 333,616          | 12,000   | 1,172                     | 13,172| 75,000               |
| RVS 5 → DVS 1    | 1    | 333,616          | 10,000   | 3,465                     | 13,465| 25,000               |
| DVS 1 → Clinic 1 | 1    | 26,704           | 5,000    | 0                         | 5,000 | 15,000               |
| DVS 1 → Clinic 2 | 1    | 26,704           | 5,000    | 0                         | 5,000 | 15,000               |
| DVS 1 → Clinic 3 | 1    | 26,704           | 5,000    | 638                       | 5,638 | 15,000               |
| DVS 1 → Clinic 4 | 1    | 26,704           | 5,000    | 424                       | 5,424 | 15,000               |
| DVS 1 → Clinic 5 | 1    | 26,704           | 5,000    | 0                         | 5,000 | 15,000               |
| DVS 1 → Clinic 6 | 1    | 26,704           | 5,000    | 413                       | 5,413 | 15,000               |
| DVS 1 → Clinic 7 | 1    | 26,704           | 5,000    | 649                       | 5,649 | 15,000               |
| DVS 1 → Clinic 8 | 1    | 26,704           | 5,000    | 363                       | 5,363 | 15,000               |
| DVS 1 → Clinic 9 | 1    | 26,704           | 5,000    | 0                         | 5,000 | 15,000               |
| DVS 1 → Clinic 10| 1    | 26,704           | 5,000    | 499                       | 5,499 | 15,000               |
| DVS 1 → Clinic 11| 1    | 11,096           | 5,000    | 5,430                     | 10,430| 15,000               |
| DVS 1 → Clinic 12| 1    | 11,096           | 5,000    | 5,430                     | 10,430| 15,000               |
| DVS 1 → Clinic 13| 1    | 11,096           | 5,000    | 5,705                     | 10,705| 15,000               |
| DVS 1 → Clinic 14| 1    | 11,096           | 5,000    | 587                       | 10,587| 15,000               |
| DVS 1 → Clinic 15| 1    | 11,096           | 5,000    | 5,454                     | 10,454| 15,000               |
| DVS 1 → Clinic 16| 1    | 11,096           | 5,000    | 5,430                     | 10,430| 15,000               |

This is seen because we have assumed a vaccine delivery lead time of 1 week from DVSs to clinics, and we also assume that one week is required to prepare a newly arrived batch of vaccines at the clinic level so that it is ready for administration to the set of eligible recipients served at that clinic. Therefore, there is a delay of two weeks before the first set of doses get administered. In order to avoid this delay and the consequent shortage costs that are incurred, an analyst using this model can simply set the planning horizon to begin the required number of time periods (depending upon the lead times associated with vaccine delivery from one tier to the next lower tier) before the actual demand is incurred, and can set the demand during this ‘lead time’ period to be zero. We also note that our current assumption of lead times at only the DVS and clinic level is only to illustrate the impact of lead times on the shortage patterns across the planning horizon; depending upon the vaccine ordering, transportation and vaccine administration patterns, lead times may need to be incorporated at other tiers also.

4.1.2. Impact of storage and transportation capacities on vaccine shortage patterns

We also note that even at low capacities, the proportion of eligible recipients in each subgroup not receiving the vaccines is the lowest in the highest priority (or most vulnerable) subgroup (0% in elderly) and the highest in the lowest priority subgroup (close to 100%) at lower fractions of available capacity. In other words, the subgroup with a higher shortage cost (a proxy for higher vulnerability, and therefore, higher priority for vaccination) is always catered to first, after which other subgroups are considered.
in conjunction with vaccine efficacies and their costs might become characteristics might be present, implying that using shortage costs for the vaccine itself, its holding cost, ordering cost, transportation costs, etc. The interplay between the shortage costs, efficacy, and all the associated costs listed above may prove difficult to unravel without a formulation such as that we present here. Further, we included it as a placeholder for the case where the single vaccine formulation is extended to consider multiple vaccines for multiple diseases. In this case, similar or overlapping subgroups on the basis of demographic characteristics might be present, implying that using shortage costs in conjunction with vaccine efficacies and their costs might become necessary to determine the optimal set of vaccines and the associated subgroups to vaccinate.

4.1.3. Impact of storage and transportation capacities on optimal inventory patterns

We also briefly discuss the impact of cold chain point and transportation capacity on the inventory pattern across the cold chain. At lower values, since the shortages are very high, the number of vaccines ordered at each tier is very less, which subsequently results in lower inventory levels. At higher values, since the capacity of vehicles is now higher, given the fact that more numbers of vaccines can be transported in fewer orders due to the high capacities, the algorithm tries to transport all the vaccines further to the next level as soon as it receives the order leading to zero inventory levels at all tiers. As we decrease the value of this parameter from the higher end, due to the reduced vaccine transportation capacities across tiers, it gets stored in the inventory and hence inventory level increases. Higher levels of inventory are seen for the GMSD and the SVS compared to the other CCPs due to the higher ordering costs at these cold chain tiers. These results are illustrated in Figs. 3(b) and 3(c), wherein the inventory patterns at the SVS and the clinics are depicted for multiple levels of cold chain capacity available for the vaccine in question. Note that the pattern described above – inventory being lower at higher capacities and higher at lower capacities – holds clearly for the SVS, but there

| Route    | Ordering pattern | Week | Quantity | Transportation costs (INR) | Ordering costs (INR) |
|----------|------------------|------|----------|----------------------------|---------------------|
| M → GMSD |                  | 1    | 333,616  | 40,000                      | 54,000              |
| GMSD → SVS |                | 1    | 333,616  | 20,000                      | 27,700              |
| SVS → RVS 5 |               | 1    | 171,520  | 12,000                      | 13,172              |
| SVS → RVS 6 |               | 1    | 162,296  | 1,248                       | 13,248              |
| RVS 5 → DVS 1 |            | 1    | 171,320  | 10,000                      | 11,300              |
| RVS 6 → DVS 2 |            | 1    | 162,296  | 10,000                      | 11,300              |
| DVS 1 → Clinic 1 |          | 1    | 26,704   | 0                           | 5,000               |
| DVS 1 → Clinic 2 |          | 1    | 26,704   | 0                           | 5,000               |
| DVS 1 → Clinic 3 |          | 1    | 26,704   | 0                           | 5,000               |
| DVS 1 → Clinic 4 |          | 1    | 26,704   | 0                           | 5,000               |
| DVS 2 → Clinic 1 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 2 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 3 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 4 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 5 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 6 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 7 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 8 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 9 |          | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 10 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 11 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 12 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 13 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 14 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 15 |         | 1    | 11,096   | 0                           | 5,000               |
| DVS 2 → Clinic 16 |         | 1    | 11,096   | 0                           | 5,000               |

| Clinic    | Weeks | Number of shortages | Total shortage cost (INR) |
|-----------|-------|---------------------|--------------------------|
| GMSD, SVS, RVS, DVS | 0 | 0 |
| Clinics 1–10 | 2; 3; 4; 5 | 26,704; 20,028; 13,352; 6,676 | 20,028 |
| Clinics 11–16 | 2; 3; 4; 5 | 11,096; 8,322; 5,548; 2,774 | 8,322 |

| Clinic    | Weeks | Number hired | Number fired | Staff numbers |
|-----------|-------|--------------|--------------|---------------|
| GMSD, SVS, RVS, DVS | All | 0 | 0 |

(d) Vaccination staffing pattern across the planning horizon: number of health workers hired, fired, and total staff numbers at the clinics.
is more variation in this pattern for the clinics. This is because of the lower ordering and transportation costs at the clinic from the DVSs compared to the higher tiers, due to which it can afford to place orders more often at certain cold chain and transportation capacities. The inventory level at the clinic then rises because of the administration lead time.

4.1.4. Impact of manufacturer’s capacity on optimal vaccine distribution: single vaccine case

In this section, we discuss the manufacturer’s capacity on the optimal vaccine distribution patterns across the cold chain. We note before proceeding with the discussion that an 8 week planning horizon was used for these sets of numerical experiments. It has been evident from COVID-19 vaccination programs across the world that the capacity of the manufacturer to meet the demand has been a significant factor in the success of the vaccination program, and hence we examine its impact on logistical considerations across the vaccine cold chain as well. From Fig. 4, we observe that when the manufacturing capacity is very low, the optimal solution satisfies the demand of a limited number of clinics, selected because they represent the shortest routes across the cold chain network, to minimize the ordering and the transportation costs. Further, only the demand of the subgroup with the highest priority (elderly recipients) is met due to limited manufacturing capacity. Given the limited manufacturer capacity (especially when the total capacity is less than that required for a subgroup in a single period), instead of transporting vaccines as they become available, vaccine doses are accumulated at the GMSD in each period until the inventory becomes sufficiently high to meet the demand of that subgroup in the limited number of clinics. These are then transported across the cold chain to the clinics without inventory accumulation at the CCPs in the intermediate tiers (i.e., inventory held is zero at all tiers where lead times are zero). Note that the clinics are selected in this situation on the basis of whether they are part of the shortest routes across the cold chain network; however, if clinics are to be prioritized due to some other criteria that become relevant at the time of decision-making (e.g., disease outbreak is high in the catchment area of a particular set of clinics), then any of the associated costs with those clinics (fixed or variable transportation or ordering costs) can be altered to ensure higher priority for the clinics in the catchment area of interest.

We notice that when the manufacturing capacity is sufficient, the optimal solution yielded by the model holds inventory at lower and intermediate tiers as the ordering and transportation costs from these are significantly lesser than those at higher tiers. Contrary to the case with very low manufacturing capacity, we see from Figs. 4(c) and 4(e) that as the manufacturing capacity increases, the inventory levels at the clinics increase from zero while the same decrease to zero at GMSD. The intermediate tiers (SVS, RVS, DVS) hold inventory at initial time periods when the capacity is sufficient to do so, which is depicted in yellow in Figs. 4(b)–4(d).

We now present the computational experiments from the multiple vaccine model.

4.2. Multiple vaccine model

4.2.1. Overview of analyses and model outputs

As done for the single commodity model, we begin our analysis for the multiple vaccine model with two cases: first with lower packed volumes per dose for each vaccine considered in the model, and a second case with higher packed volumes per dose for each vaccine. We consider two vaccines, which differ in their packed vaccine volume per dose, efficacy and cost of administration. Assuming sufficient manufacturing capacity, lead times of 1 week for delivery to the clinics from the DVS and preparation/administration at the clinics, we run the model for two sets of packed volumes:

- Lower packed volume per dose.
- Higher packed volume per dose.

We now illustrate how the multiple vaccine model can be used to determine the conditions under which the higher efficacy vaccine is not administered. We begin by analyzing the impact of manufacturer capacity. It can be seen from Fig. 5 that even at low manufacturing capacities, the higher efficacy vaccine is delivered to its full capacity — that is, if the manufacturer is able to deliver 100 doses at the beginning of week , all 100 doses are delivered. The remainder of the demand is fulfilled by the lower efficacy vaccine. We see that it is only at extremely low values of the manufacturer’s capacity (above 10 units per week) that minimizing the costs of ordering two vaccines are prioritized lower than minimizing the shortage costs, and hence the lower efficacy vaccine units are also ordered to meet the demand requirement. It is unlikely that the situation depicted in this graph is likely to realistically occur at the figures observed; however, depending upon the differences in ordering, transportation and storage costs, such a situation may come to pass at significantly higher manufacturer capacities. This analysis provides an illustration of how our model can be used to determine the threshold capacity of the manufacturer of the higher dose vaccine below which the lower efficacy vaccines are also selected for administration.

We now investigate the impact of costs per dose of the vaccines considered in this model. While the vaccine with higher efficacy yields a lower shortage cost, its cost per dose could be greater than that of the vaccine with lower efficacy. The multiple vaccine model can be used to determine the difference in the costs of the two vaccines at which the vaccine with the lower efficacy administered, given the sufficient manufacturer capacity for both the vaccines. We illustrate this now. In this analysis, we keep all the costs for the two vaccines same except for

Vaccine 1: packed volume per dose of 0.211 cm$^3$/dose, efficacy 93.7%, and cost per dose INR 780.
Vaccine 2: packed volume per dose of 0.086 cm$^3$/dose, efficacy 77.8%, and cost per dose INR 1410.

### Higher packed volume per dose.
- Vaccine 1: packed volume per dose of 3.3 cm$^3$/dose, efficacy 93.7%, and cost per dose INR 780.
- Vaccine 2: packed volume per dose of 1.719 cm$^3$/dose, efficacy 77.8%, and cost per dose INR 1410.

We observe that, as expected, with sufficient manufacturer capacity for both vaccines, the optimal solution from the multiple vaccine model reduces to that obtained from the single vaccine model. This is because all other parameter values — such as ordering, inventory holding, and fixed and variable transportation costs — are assumed to be the same for both vaccines, and the difference in the costs per dose of the vaccines is not high enough compared to the shortage cost (as is likely to be the case) to prevent the higher efficacy vaccine to be administered. Thus we see that the higher efficacy — to be precise, the vaccine with the higher shortage cost — is selected for administration to the recipients.

In the current multiple vaccine formulation, we have used only a single efficacy parameter for the vaccines. However, vaccine efficacy may be measured with respect to multiple clinical endpoints: for example, efficacy in preventing symptomatic disease, in reducing transmission, in preventing severe disease and/or hospitalization, or in preventing death. Costs can be associated with each of these endpoints to arrive at a more comprehensive measure of vaccine efficacy. Further, some vaccines can be significantly more expensive to store or transport, and even ordering costs can be significantly higher, especially if both domestically manufactured vaccines and imported vaccines are considered for the same group of recipients. While we reserve the consideration of these complexities for future research, our work provides a proof-of-concept for how these considerations can be integrated within a decision support framework for optimizing vaccine distribution across the cold chain network.

4.2.2. Impact of manufacturer’s capacity, vaccine costs and vaccine efficacy on optimal vaccine choice

We now illustrate how the multiple vaccine model can be used to determine the conditions under which the higher efficacy vaccine is not administered. We begin by analyzing the impact of manufacturer capacity. It can be seen from Fig. 5 that even at low manufacturing capacities, the higher efficacy vaccine is delivered to its full capacity — that is, if the manufacturer is able to deliver 100 doses at the beginning of week , all 100 doses are delivered. The remainder of the demand is fulfilled by the lower efficacy vaccine. We see that it is only at extremely low values of the manufacturer’s capacity (above 10 units per week) that minimizing the costs of ordering two vaccines are prioritized lower than minimizing the shortage costs, and hence the lower efficacy vaccine units are also ordered to meet the demand requirement. It is unlikely that the situation depicted in this graph is likely to realistically occur at the figures observed; however, depending upon the differences in ordering, transportation and storage costs, such a situation may come to pass at significantly higher manufacturer capacities. This analysis provides an illustration of how our model can be used to determine the threshold capacity of the manufacturer of the higher dose vaccine below which the lower efficacy vaccines are also selected for administration.

We now investigate the impact of costs per dose of the vaccines considered in this model. While the vaccine with higher efficacy yields a lower shortage cost, its cost per dose could be greater than that of the vaccine with lower efficacy. The multiple vaccine model can be used to determine the difference in the costs of the two vaccines at which the vaccine with the lower efficacy administered, given the sufficient manufacturer capacity for both the vaccines. We illustrate this now. In this analysis, we keep all the costs for the two vaccines same except for

Vaccine 1: packed volume per dose of 0.211 cm$^3$/dose, efficacy 93.7%, and cost per dose INR 780.
Vaccine 2: packed volume per dose of 0.086 cm$^3$/dose, efficacy 77.8%, and cost per dose INR 1410.

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In the current multiple vaccine formulation, we have used only a single efficacy parameter for the vaccines. However, vaccine efficacy may be measured with respect to multiple clinical endpoints: for example, efficacy in preventing symptomatic disease, in reducing transmission, in preventing severe disease and/or hospitalization, or in preventing death. Costs can be associated with each of these endpoints to arrive at a more comprehensive measure of vaccine efficacy. Further, some vaccines can be significantly more expensive to store or transport, and even ordering costs can be significantly higher, especially if both domestically manufactured vaccines and imported vaccines are considered for the same group of recipients. While we reserve the consideration of these complexities for future research, our work provides a proof-of-concept for how these considerations can be integrated within a decision support framework for optimizing vaccine distribution across the cold chain network.
We see from Fig. 6(a) that when the difference between the cost of vaccine is less than INR 19,300, it is always the higher efficacy vaccine that is administered but beyond this, some doses of the lower efficacy vaccine are also administered.

We see that once this threshold difference in costs per dose between the vaccines is breached, the cost of the higher efficacy vaccine dominates the shortage cost for the subgroup comprising children, but does not do so for the adult and elderly subgroups due to their shortage costs and costs per dose.
higher shortage costs. Hence, the demand for the subgroup comprising children is met by the lower efficacy vaccine while the other subgroups receive the higher efficacy vaccine. When the cost per dose difference exceeds INR 25,200, adults also receive the lower efficacy vaccine, and when it exceeds INR 28,600, all recipients receive the lower efficacy vaccine.

Once again, we note that while it is very unlikely that vaccines will differ in their costs per dose by as much as INR 19,300, the lower efficacy vaccine may be preferred if differences in other associated costs are also significantly higher for the higher efficacy vaccine, and the vaccine efficacies are not substantially different. This is illustrated in Fig. 6. In this analysis, we increased key fixed and variable costs that...
could conceivably be greater for the higher efficacy vaccine (e.g., the cost per dose, the inventory holding and fixed ordering costs), and we find that when these costs are 9 times that of the lower efficacy vaccine, the lower efficacy vaccine starts receiving orders. As the vaccines become closer in efficacy, the value of this multiplier will also accordingly decrease. This is illustrated in Fig. 7, where we show how the ratio of vaccine ordering and holding costs for the higher and lower efficacy vaccines decreases almost linearly as they become closer in efficacy. However, even at a vaccine efficacy difference of 4%, we see that the value of this ratio is approximately 8 for the least vulnerable subgroup, implying that the prioritization of the health outcomes of vulnerable subgroups is achieved effectively via this framework.

In summary, the above set of numerical experiments represent a comprehensive demonstration of the variety of what-if scenario and sensitivity analyses that can be conducted via the models in the decision support framework. In conducting these analyses, we have explicitly examined the impact of changing almost all key model parameters: these include storage and transportation capacities, manufacturing capacity, vaccine holding and carrying costs, and vaccine purchase costs. Implicit analysis of the shortage costs has been conducted as part of other analyses — for example, in the multiple vaccine case where manufacturing capacity for the higher efficacy vaccine was reduced to a low level. From these analyses, it is apparent that it is the relative difference in shortage costs between recipient subgroups that drives vaccine choice for each subgroup.

5. Discussion & conclusions

We present in this paper a decision support framework for optimal vaccine distribution across the vaccine cold chain network. We present two integer linear programming models within the framework: a model considering a single vaccine for a single disease, and a model considering multiple vaccines for a single disease. The model can be extended to incorporate multiple vaccines for multiple diseases as well. Finally, we develop two robust optimization formulations for the single vaccine model: one with box uncertainty sets and the other with budgeted uncertainty sets. As discussed in Section 2, a key advantage of our optimal vaccine distribution framework is that it only contains...

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Table A.3

| Initial data required for estimation of capacities. |
|---------------------------------------------------|
| No of CCE units in Bihar (Ministry of Health and Family Welfare, 2017) |
| WIF (Walk in Freezer) | 3 |
| WIC (Walk in Cooler) | 17 |
| ILR (In-line Refrigerator) | 1039 |
| DF (Deep Freezer) | 887 |
| Miscellaneous (World Health Organization, 2017) |
| Utilization factor | 0.67 |
| Standard dimensions of vehicle storage areas\(^a\) |
| Length (cm) | 244 |
| Breadth (cm) | 229 |
| Height (cm) | 259 |
| Standard dimensions of cold boxes\(^a\) |
| Length (cm) | 54.4 |
| Breadth (cm) | 44.5 |
| Height (cm) | 42 |

\(^a\)The dimensions are estimated based on the commercially available trucks and cold boxes in India taken from [https://www.indiamart.com/](https://www.indiamart.com/)
end. Preprocessing can also be included automatically to a certain
terms will automatically be omitted from the formulation in the back-
exclude vaccination staffing decisions, in which case the appropriate
sets of decisions in their analysis: for example, they may choose to
analyst will also be able to choose whether to include or exclude certain
formulations. Further, the analyst will have the option of deciding
whether to include or exclude a particular cold chain tier from their
or the multiple vaccine model; or to use the robust versions of these
support tool in a modular form. This implies that the tool will allow
planning vaccine distribution across the cold chain. Therefore, we
intend to incorporate this framework within a computational decision
works within public health systems across the world (as discussed in
reflect the disparity in efficiency in their respective ordering processes.
facilities can be adjusted (starting from a reasonable initial estimate) to
than at comparable tiers or facilities, then the ordering costs for these
tier (e.g., clinics in a particular district), is significantly more efficient
cold chain tier, or a particular group of facilities within a cold chain
discussed in the preceding sections, it is the relative value of these
vaccine distribution; hence for analysts working in these organizations,
parameters that are more relevant than actual estimates themselves.
estimating these parameters may be a one-time effort. Further, as
discussed in the preceding sections, it is the relative value of these
parameters that are more relevant than actual estimates themselves.
Further, the analyst may not have access to primary data required to estimate inventory holding costs for a
vaccine at every cold chain point within the network. However, we note
that such data may be available to public health authorities overseeing vaccine distribution; hence for analysts working in these organizations, estimating these parameters may be a one-time effort. Further, as discussed in the preceding sections, it is the relative value of these parameters that are more relevant than actual estimates themselves.
For example, if it is known that the ordering process at a particular

component accompanying this article can automatically be deployed.
then preprocessing techniques such as those discussed in the electronic
device accompanying this article can automatically be deployed.
unit accompanying this article can automatically be deployed.
facilities can be adjusted (starting from a reasonable initial estimate) to
than at comparable tiers or facilities, then the ordering costs for these
tier (e.g., clinics in a particular district), is significantly more efficient
cold chain tier, or a particular group of facilities within a cold chain
discussed in the preceding sections, it is the relative value of these
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vaccine at every cold chain point within the network. However, we note
that such data may be available to public health authorities overseeing vaccine distribution; hence for analysts working in these organizations, estimating these parameters may be a one-time effort. Further, as discussed in the preceding sections, it is the relative value of these parameters that are more relevant than actual estimates themselves.
For example, if it is known that the ordering process at a particular
cold chain tier, or a particular group of facilities within a cold chain
tier (e.g., clinics in a particular district), is significantly more efficient
than at comparable tiers or facilities, then the ordering costs for these
facilities can be adjusted (starting from a reasonable initial estimate) to
reflect the disparity in efficiency in their respective ordering processes.
Overall, given the ubiquity of multi-tier vaccine cold chain net-
works within public health systems across the world (as discussed in
Section 1), we believe that the decision support framework that we
propose in this study can be useful for stakeholders within public health
planning authorities in these health systems.
Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Model parameterization: supplementary information

Preliminary parameters used in the estimation of optimization formulation parameters (see Section 3.4 for a description of how these model parameter estimates are derived) are provided in Table A.3.

The final set of parameters for the optimization models in our decision support framework are given in Table A.4.

Appendix B. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.cie.2023.109397.

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The final set of parameters for the optimization models in our decision support framework are given in Table A.4.

Appendix B. Supplementary data

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