Vaccine network design to maximize immunization coverage

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Abstract

Purpose – The COVID-19 pandemic has forced countries to consider how to reach vulnerable communities with extended outreach services to improve vaccination uptake. The authors created an optimization model to align with decision-makers' objective to maximize immunization coverage within constrained budgets and deploy resources considering empirical data and endogenous demand.

Design/methodology/approach – A mixed integer program (MIP) determines the location of outreach sites and the resource deployment across health centers and outreach sites. The authors validated the model and evaluated the approach in consultation with UNICEF using a case study from The Gambia.

Findings – Results in The Gambia showed that by opening new outreach sites and optimizing resource allocation and scheduling, the Ministry of Health could increase immunization coverage from 91.0 to 97.1% under the same budget. Case study solutions informed managerial insights to drive gains in vaccine coverage even without the application of sophisticated tools.

Originality/value – The research extended resource constrained LMIC vaccine distribution modeling literature in two ways: first, endogenous calculation of demand as a function of distance to health facility location enabled the effective design of the vaccine network around convenience to the community and second, the model's resource bundle concept more accurately and flexibly represented complex requirements and costs for specific resources, which facilitated buy-in from stakeholders responsible for managing health budgets. The paper also demonstrated how to leverage empirical research and spatial analysis of publicly available demographic and geographic data to effectively represent important contextual factors.

Keywords Vaccine, Immunization, Network design, Humanitarian healthcare supply chains, Endogenous demand

Paper type Research paper

1. Introduction

Vaccine supply chains have received significant attention given their vital role in addressing the COVID-19 pandemic. Incredible effort was exerted to rapidly develop, manufacture and distribute COVID-19 vaccines. The urgent need to reach every person has revealed gaps in providing access to vaccination services for all communities. There is renewed global awareness that vaccine supply chains must extend into every community with sufficient physical and human resources to provide convenient and trustworthy vaccination services.

Though vaccine supply chain has appropriately focused on COVID-19 outbreak response, attention must also remain on support for routine immunizations that lagged due to the pandemic. Early in the pandemic, vaccine shipments were significantly impacted by a dramatic decline in commercial air transportation and lockdowns of receiving countries. In May 2020, a total of 99 countries reported the suspension of immunization campaigns for the following antigens: measles/measles rubella, polio (including for vaccine derived polio virus response activities), meningococcal A, yellow fever, typhoid, cholera and tetanus/diphtheria (UNICEF, 2019).

Despite remarkable progress in the reduction of child mortality through immunization, coverage for routine vaccines had stagnated even before the COVID-19 disruption. Experts at the 2019 Regional Immunization Technical Advisory Group (RITAG) meeting called for strengthened routine immunization as coverage in sub-Saharan Africa had plateaued at 72% (WHO, 2019). The COVID-19 disruptions further strained health systems such that 23 million children missed out on vaccination in 2020, 3.7 million more than in 2019 and the highest number since 2009 (WHO, 2021).

UNICEF, with a mandate to help meet children's basic needs and expand their opportunities to reach their full potential, plays a central role in vaccine supply chains. In 2019, UNICEF procured an estimated 2.43 billion doses of vaccines to around 100 countries to reach approximately 45% of the world's children under five

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(UNICEF, 2019). UNICEF has also scaled efforts for procurement and distribution of COVID-19 vaccine doses as a partner of the COVAX Facility, led by Gavi, the Vaccine Alliance, World Health Organization (WHO) and the Coalition for Epidemic Preparedness Innovations (CEPI). UNICEF also procures and transports immunization supplies such as syringes, safety boxes for their disposal, and cold chain equipment such as vaccine refrigerators. The collaboration between MIT and UNICEF that supported this research began prior to the Covid-19 pandemic. While the research was motivated to increase routine immunization coverage in Low and Middle Income Countries (LMICs), the approach to design vaccine networks with the primary objective of community outreach also applies directly to pandemic vaccination response such as for COVID-19.

Consultation with UNICEF shaped the scope of our vaccine network design efforts. Given the goal to increase community access to vaccines, we focused on distribution with the primary decisions of facility location and resource deployment. Facility location focused in outreach sites, which are single-day clinics conducted in more remote communities. Resource deployment considered both the established health centers that offer routine immunization services and the outreach sites, which are supported by staff deployed from the health centers.

Efforts to improve immunization coverage through vaccine network design must embed the realities of health system services and the behaviors of people in the communities they serve. Starting with the community, vaccine networks should improve access by striving to reach people with convenient services that are trustworthy. Vaccine uptake depends on a combination of interventions to drive demand (e.g. information dissemination, community engagement) and provide services. While we do not link demand to specific interventions, our approach explicitly ties demand with proximity to the facilities that implement them. To consider the health system realities around implementation, we modeled the deployment of specific commodities, equipment, assets, and skilled workers required by the interventions. Finally, the fundamental reality in providing health services is a constrained budget, especially in LMICs. As a result, many vaccine network design efforts focus on minimizing cost. However, given our research aim to increase access, our objective function focused on providing access to community members while respecting the budgetary constraints.

Based on the motivation and context, the study sought to answer the following questions:

1 How can vaccine distribution networks be designed to maximize immunization coverage given budget constraints?
2 How does the proximity of population to vaccination services affect the immunization coverage?
3 How can important contextual factors that affect vaccination demand and/or resource deployment in LMICs be effectively modeled?

To optimize vaccine network design, we developed a mixed integer program (MIP) to determine the location of outreach sites and the resource deployment across health centers and outreach sites. Our research extended the vaccine distribution modeling literature with two novel contributions. First, the model included a general function for endogenous calculation of demand based on network design decisions such as distance to vaccination locations. Second, the model's resource bundle concept more accurately and flexibly represented complex resource requirements and costs to facilitate buy-in from stakeholders responsible for managing health budgets.

We validated the model and evaluated the approach in consultation with UNICEF using empirical data from The Gambia. While we did not develop further evidence linking immunization coverage with proximity of population to vaccination services, we calibrated the model's endogenous demand function to the country context and conducted sensitivity analysis with the demand function. Results show the potential to increase immunization coverage from 91.0% to 97.1% under the same budget through better deployment of equipment and staff across existing health centers and support for more outreach sites. The case study provided two additional contributions. First, it demonstrated how to leverage empirical research and spatial analysis of publicly available data to effectively represent important contextual factors. Second, case study solutions informed managerial insights to drive gains in vaccine coverage even without application of sophisticated tools. Thus, the research provided practical tools and insights such that LMICs specifically, and public health agencies more generally, can more easily pursue evidence-driven improvements to vaccine distribution in various contexts.

The paper is organized as follows: a review of literature on vaccine network design and immunization demand in Section 2 informs our methodology described in Section 3. A case study of The Gambia in Section 4 informs research and managerial insights discussed in Section 5. We conclude in Section 6.

2. Literature review

This literature review is organized around our research questions. Although research on network design is abundant, we focused our literature review on models that address context of vaccine networks and compare studies based on a set of criteria relevant to this problem. Next, we explored the health literature to characterize research on the impact of proximity on demand. Finally, we outlined contextual factors with potential impacts on demand and how this topic could be further explored. We close by identifying research gaps to position our work.

2.1 Vaccine distribution network design

Two prior studies categorized optimization models for vaccine network design. Lemmens *et al.* (2016) characterized studies of network design by the type of problem they aimed to solve, creating the following framework: (1) demand allocation; (2) vaccination location; (3) production capacities, and (4) batch sizes. A more recent work (Duijzer *et al.*, 2018), used four different components for classification, similarly focusing on the problem being solved: (1) product; (2) production; (3) allocation; and (4) distribution. Although the naming of the categories is different, we found similarities. For example, vaccination location (Lemmens *et al.*, 2016) is similar to distribution (Duijzer *et al.*, 2018) as the decision of where a vaccination center should be located is intrinsically connected to how vaccines are distributed.

Our research problem fell within this combined category, distribution and vaccination location. Our work with UNICEF specifically focused on the LMIC context, though the approach is generally applicable. For LMIC vaccine networks, it is reasonable to assume that the product and production decisions, such as who will supply vaccines and how many doses of what type will be made available, are made by national government planners (Chen *et al.*, 2014). Moreover, the allocation decision, such as who should receive the vaccine, is not pertinent to our research objective to maximize the access to immunization. According to Chen *et al.* (2014), the basic structure of vaccine supply chains in LMIC follows a similar structure, with a central storage location that serves as a supplier to a multi-layered chain formed by regional stores/hubs and clinics. With the product, production, and allocation decisions out of scope, our literature review focused on vaccine distribution in LMIC.

We identified six highly relevant papers to the specified topic. To establish a methodology of comparing these six works, we defined the following criteria for classification:

1 Objective: Minimize costs and maximize access to vaccine
2 Decisions: Locations, flow between nodes, inventory level, vehicle types, storage types and other relevant characteristics.
3 Network structure: Central distribution, hubs, clinics and outreach sites
4 Demand: Fixed exogenous, stochastic and causal endogenous (distance based function)
5 Product: One vaccine and multiple vaccines
6 Period: Single and multi-period
7 Constraints: Vehicle/storage capacities and maximal distance

Our classification criteria built on the three types of decisions in the distribution phase of vaccine supply chains proposed by Duijzer *et al.* (2018): (1) the design of the supply chain – number of layers and its locations; (2) the inventory control policy – size and location of stock; and (3) the dispensing points. We added details in our criteria to further differentiate existing models and identify gaps. A summary matrix below illustrates the different characteristics (Table 1). For the clarity of analysis, we divided the six papers into two groups based on the strong connection among the works.

In this first group, we clustered three papers that do not consider outreach sites. Chen *et al.* (2014) built a general mathematical model to optimize operations in vaccine networks in LMIC. They proposed a formulation that considers a multi-period capacitated network model with different types of storage devices, vehicles, and vaccines types with the introduction of the vaccination regimen concept that determines how many doses of each vaccine type a child must receive to be considered fully immunized.

Building upon the work done by Chen *et al.* (2014), Lim (2016) proposed a model to redesign vaccine distribution networks in LMIC. This paper did not have the multiple vaccine complexity of Chen *et al.* (2014), but did consider the decision to open locations, combined with other more operational aspects, in formulating a MIP to minimize cost. Due to this complexity, a novel hybrid algorithm based on MIP and an evolutionary strategy was developed.

Yang *et al.* (2021) built upon (Lim, 2016) by adding complexities to the model such as flexible sizes of storage devices and a single trip constraint on deliveries. Once again, problem complexity and size made it necessary to create a disaggregation-and-merging algorithm.

Although these papers were a potential source of operational constraint enhancements, they considered exogenous demand and required a complex solution methodology. Most critically, none of them incorporated outreach sites where health care professionals are regularly sent from fixed clinics to operate one-day clinics in villages to vaccinate the nearby population. Interviews with UNICEF revealed that vaccination through outreach sites is highly relevant for immunization efforts in LMIC. The Reaching Every District strategy (RED) established by UNICEF and its partners aims to develop vaccination delivery strategies that reach more of the target population (Vandelaer *et al.*, 2008). Thus, the second group of three works incorporating outreach sites is more closely related to our work.

Lim *et al.* (2016) contained the first quantitative model to determine optimal outreach trips and policies to maximize coverage. This work also considered the distance impact in coverage – one of our research questions. Their main decisions were the location of outreach sites and which fixed clinics should serve as a base for outreach operations. An important assumption of this modeling was that each outreach sites was located at a given and constrained, i.e. maximum, Euclidean distance from fixed clinics. They did not consider candidate sites throughout the region identified by systems of access, such as road networks.

Mofrad (2016) extended (Lim *et al.*, 2016) by combining health center location and outreach planning while including vaccinations at health centers. Using a different solution approach, this model treated outreach planning as a vehicle routing problem. In practice, this further limits the number of vaccines each outreach location can receive from a single trip. The formulation included stochastic demand but did not consider causal demand based on population distance. The modeling approach in the third paper (Yang and Rajgopal, 2019) was very similar to Mofrad (2016), with the addition of a time aspect into the outreach trip planning. In this sense, the work by Yang and Rajgopal (2019) can be seen as a vehicle routing problem with time windows (VRPTW) combined with a set-covering problem (SCP).

The models proposed by Mofrad (2016) and Yang and Rajgopal (2019) added significant complexity to the modeling of Lim *et al.* (2016) with the incorporation of routing aspects to outreach trips, clinic location decisions, and service levels. However, both papers excluded an important aspect of Lim *et al.*'s (2016) formulation: formal incorporation of the effect of distance on immunization demand. In addition, planning outreach as a vehicle routing problem was not an operational aspect raised by our stakeholders. Finally, the health center opening decision was irrelevant to our model since these locations were treated as fixed.

Following the criteria established at the beginning of this section and presented in Table 1, we defined our model characteristics as follows:

1 Objective: Maximize access to vaccine
2 Decisions: Open outreach; service level at fixed clinics
3 Network structure: Clinics and outreach sites
4 Demand: Causal and endogenous
5 Product: Single vaccine
6 Period: Single period
7 Constraints: Maximum distance between outreach and fixed clinics

2.2 Distance effect on vaccination coverage

Our second research question explored the impact of proximity on vaccination coverage. The relevance of including this factor was quantitatively assessed by Blanford *et al.* (2012). After conducting a study in Niger, their results showed a 95% significance level that the probability of children living an hour from vaccination facilities being fully immunized at one year old is 1.88 higher than children living in more distant areas. Ibnouf *et al.* (2007) explored how time influences immunization demand among children under five in Sudan. Children of mothers who

Table 1 Comparison of key characteristics of previous vaccine network models

	Group 1 - No outreach locations			**Group 2 - outreach locations**		
	1. Chen *et al.* (2014) A planning model for the WHO-EPI . . .	**2. Lim (2016) Improving the design and operation . . .**	**3. Yang *et al.* (2021) Optimizing vaccine distribution networks . . .**	**4. Lim *et al.* (2016) Coverage models to determine outreach . . .**	**5. Mofrad (2016) Optimizing vaccine clinic operations . . .**	**6. Yang and Rajgopal (2019) Outreach strategies for vaccine distribution . . .**
Objective						
Maximize coverage	Maximize coverage			Maximize coverage		
Minimize costs		Minimize costs	Minimize costs		Minimize costs	Minimize costs
Decisions						
Open locations		Open hub	Open hub	Open outreach	Open outreach and clinic	Open outreach and clinic
Flow between nodes	Flow between nodes	Vehicle types and number	Vehicle types and number			
Vehicle types	Vehicle types	Vehicle types	Vehicle types		Vehicle types and outreaches	
Storage types	Storage types	Storage types	Storage types			
Inventory levels	Inventory levels	Inventory levels	Inventory levels			
Outreach routes					Number of outreach trips	Number of outreach trips
Capacity			Variable device capacity			
Network structure						
Central distribution	Central distribution	Central distribution	Central distribution			
Hubs	Hubs	Hubs (variable)	Hubs (variable)			
Clinics	Clinics	Clinics	Clinics	Clinics	Clinics (variable)	Clinics (variable)
Outreaches				Outreaches	Outreaches (variable)	Outreaches (variable)
Demand						
Fixed exogenous	Fixed	Fixed				
Stochastic			Stochastic		Stochastic	Stochastic
Causal (distance)				Causal (distance)		
Product						
Single vaccine		Single vaccine	Single vaccine	Single vaccine	Single vaccine	Single vaccine
Multiple vaccines	Multiple vaccines					
Period						
Single period				Single period	Single period	Single period
Multiple periods	Multiple periods	Multiple periods	Multiple periods			
Constraints						
Capacity on facilities	Capacity on facilities	Capacity on facilities	Variable capacity			
Capacity on vehicles	Capacity on vehicles	Capacity on vehicles	Capacity on vehicles		Capacity on vehicles	Capacity on vehicles
Others			Single trip delivery	Dist. max outreach to fixed HC	Daily trips to one dest Patient and outreach max travel dist	Max travel time to multiple dest Patient max travel dist

have better access to vaccine services, less than 30 min walking time to the nearest place of vaccination, were about 3.4 times more likely to have correct vaccinations than were children of mothers walking 30 min or longer. Some papers studied distance-decay quantitatively. For instance, Feikin *et al.* (2009) considered resident distance from a peripheral health facility on pediatric health utilization in rural western Kenya. The rate of clinic visits decreased linearly at 0.5 km intervals up to 4 km, after which the rate was stabilized. Using Poisson regression, for every 1 km increase in distance of residence from a clinic, the rate of clinic visits decreased by 34%. Different from our research, their study was not applied to the immunization context.

Verter and Lapierre (2002) modeled the negative impacts on coverage as distance increases from clinics. Their maximal coverage location of preventive care facilities problem assumed that coverage reduced linearly with distance. Tanser (2006) and Gu *et al.* (2010) also incorporated this effect in their healthcare facility location research with similar approaches. The first paper to incorporate this specific effect in the optimization of vaccine networks models was Lim *et al.* (2016). Unlike Verter and Lapierre (2002), however, they considered the reduction of coverage to be either binary or stepwise. In our modeling, we assumed a linear decrease in demand function based on the distance, similar to what was done by Verter and Lapierre (2002).

2.3 Other factors affecting the demand

We found only one paper related to our last research question on modeling contextual factors that affect vaccination demand. Echakan *et al.* (2018) quantitatively and qualitatively assessed, through interviews of the population and health records analysis, that distance/time is a main factor in immunization access. Their work highlighted the importance of advertising outreach operations so that the target population knows when and where outreach sites will be opened. This is an intuitive piece of information that models have not directly considered.

While not focused on vaccination demand, Burkart *et al.* (2017) explored how beneficiaries' choice can improve the design of a distribution network. The authors explained that beneficiaries do not necessarily follow the assumed assignment of relief goods demand to the nearest distribution centers. Although the context of this study was the distribution of relief goods after a disaster rather than regular vaccination activities, it is important to note that beneficiaries might prefer to visit a location other than the nearest one. Capturing and incorporating information on the potential attractiveness of potential sites could result in improved model performance. Such efforts could be incorporated through a different demand function, which our model could incorporate.

In addition, from discussions with UNICEF, the quality of human resources, especially at outreach locations, significantly affects vaccine demand. Human resources includes both the skilled health professionals and unskilled volunteers. If their morale, as well as their quality of work, are high, more people will tend to get vaccinated. It is not yet clear, however, how these effects can be incorporated into optimization models.

2.4 Literature gaps

Much of the vaccine network design research focused on cost minimization and did not explicitly model the causality between design decisions and immunization demand. Engagement with stakeholders confirmed the centrality of designing operations to maximize immunization coverage given a constrained budget. From the papers relevant to our problem only (Lim *et al.*, 2016) focused on both maximizing coverage and modeling casual demand and is most relevant to our work. Our model extends (Lim *et al.*, 2016) in the following ways. First, we explicitly modeled the ability of fixed clinics to serve the population. Second, we incorporated flexible capacity at the fixed clinics as decision variables by varying the number of employees or working hours. Third, we defined candidate outreach sites based on road networks rather than Euclidean distance. Fourth, we tailored cost functions for both fixed clinics and outreach sites that combine fixed and variable costs in representing realistic resource bundles. Finally, we incorporated a generic demand function instead of requiring a stepwise function.

3. Research methodology

We aimed to support a government's strategic decisions in terms of budget for vaccination campaigns as well as a structured and optimized way to determine the location of the vaccination points. It was not the objective of this model to provide a daily schedule of how to operate the network, and for this reason, we did not follow the location routing approach applied by Mofrad (2016) and Yang and Rajgopal (2019).

The methodology used in this study was Mixed Integer Programming (MIP) with a formulation developed in Python using a solver to perform the MIP optimization. The objective function maximizes access to vaccination in LMIC while incorporating an endogenous demand function into the model. To develop this model, we followed a multi-setup approach by first defining an exploratory model to facilitate interaction with UNICEF in formulating the formal model to use with empirical data from The Gambia.

3.1 Exploratory model

Based on the literature review and initial discussions with UNICEF Supply Division, we developed an exploratory model for a small-scale problem with fabricated data. Researchers could explain the model and share dynamics with an easily understood problem that facilitated stakeholder feedback to improve the model design (see Figure 1 for a visual depiction).

The objective function of the exploratory model was to maximize immunizations in either fixed health centers or outreach sites subject to a constrained budget. Fixed health centers were established locations that offer routine immunization services and outreach sites were single-day clinics conducted in more remote communities by people sent from fixed health centers. The demand for immunization was modeled as an endogenous function that reflects people's willingness or capacity to travel for immunization services. Decision variables included the number of employees at the fixed health centers and the candidate outreach sites to open.

Discussion of the exploratory model centered on scenarios tied to three input factors – outreach implementation costs, health center employee costs, and the demand function. Exploratory model interaction with UNICEF Supply Division identified two important model improvements. The first was that the outreach sites' size should vary depending on the resources used. The second was that the costs of an outreach operation should not be variable and based on the operation size and distance from its supplying facility. Validation of the demand function based on health expert experiences was also an important development.

3.2 Formal model

When exploratory model results aligned with stakeholder intuition, researchers formalized the model. The formal model formulation in this section uses the following notation.

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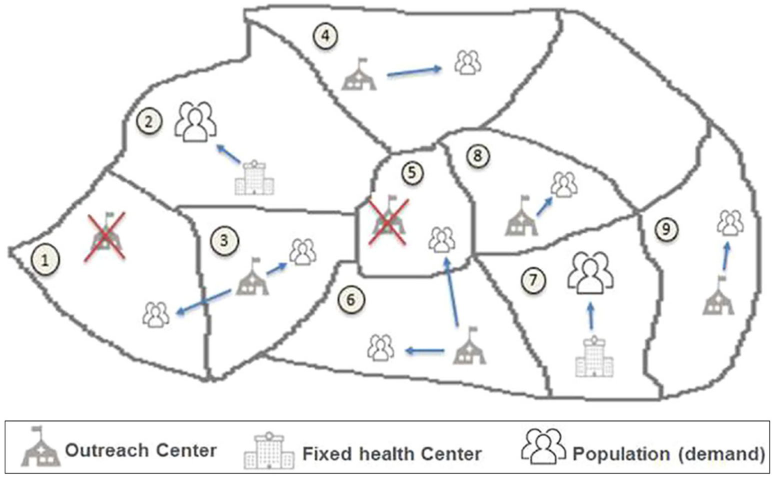
Figure 1 Exploratory model scenario



Sets

F = set of fixed health centers f
O = set of potential outreach centers o
J = set of population regions j

Variables

X_{fj} = people from region j vaccinated by fixed health center f [Continuous]
X_{oj} = people from region j vaccinated by outreach site o [Continuous]
X_{fo} = resource bundles from fixed health center f to outreach site o [Integer]

$$Y_{fj} = \begin{cases} 1 & \text{if region } j \text{ served by fixed health center } f \\ 0 & \text{if otherwise} \end{cases} \text{ [Binary]}$$

$$Y_{oj} = \begin{cases} 1 & \text{if region } j \text{ serviced by outreach site } o \\ 0 & \text{if otherwise} \end{cases} \text{ [Binary]}$$

$$X_{fj}, X_{oj}, X_{fo} \geq 0 \qquad \forall f \epsilon F, \forall o \epsilon O, \forall j \epsilon J$$

Parameters

Fixed health centers
CE_f = employee cost at fixed health center f ($/day)
PE_f = employee productivity at fixed health center f (doses/day)

Resource bundle (outreach)

CE_o = employee cost at outreach o ($/day)
PE_o = employee productivity at outreach o (doses/day)
Vp = doses per resource bundle
Ve = *max* employees per vehicle
Vcv = *max* cold boxes per vehicle
Vdc = average vaccine doses per cold box
$Dist_{fo}$ = distance between fixed health center f and outreach o (km)
C_{fo} = total resource bundle cost ($)

Demand

$\propto_{fj}$ = vaccination coverage of region j by fixed health center f
$\propto_{oj}$ = vaccination coverage of region j by outreach center o
D_j = total demand for immunization in region j
d_{fj} = doses demanded by region j filled by fixed health center f
d_{oj} = doses demanded by region j filled by outreach center o

Costs

B = total available budget ($)
Cv = cost per vaccine dose ($/dose)
Cov = vehicle operation cost per km ($/km)

3.2.1 Endogenous demand function

This research sought to answer how the proximity of outreach centers affect demand. This research began to answer that question through the incorporation of an endogenous demand function. Based on our previous work (Russell *et al.*, 2019), literature review, and conversations with stakeholders, we started from the assumption that the demand that a fixed health center f can capture from population center j, d_{fj}, decreases as the distance between f and j increases. This captured the conclusion that people would be less likely to travel for immunization services as the location for immunization becomes further away from them. Mathematically, this was formulated by multiplying the demand D_j by factor α_{fj}, as shown in Equation (7). This factor, called vaccination coverage, is a function of the distance between f and j, $\alpha_{fj} = f(\text{Dist}_{fj})$. The same approach is extended for outreach sites, as Equation (8) shows.

The key question is the shape of the function $\alpha_{fj}=f(\text{Dist}_{fj})$. As shown in the literature review, there is no consensus on the shapes and coefficients of such a function. In addition, the derivation of a demand function for a specific country requires detailed data and study. However, the literature review allowed us to arrive at reasonable estimations and boundaries on which it would be reasonable to evaluate. In The Gambia case study, we explore three demand function options.

As an example, the equation below describes a linear decay function a demand decrease of 20% every 100 km.

$$\alpha_{fj}=1-0.2\cdot\frac{\text{Dist}_{fj}}{100}\qquad \forall f\epsilon F,\ \forall j\epsilon \mathcal{J}$$

Assume fixed health center 1 is at a distance of $\text{Dist}_{12} = 200$ km to Region 2 and at a distance $\text{Dist}_{13} = 300$ km to Region 3. Using the function, the vaccine coverage would be $\alpha_{12} = 0.6$ and $\alpha_{13} = 0.4$. Assuming the total demand in the two regions is the same ($D_2 = D_3 = 500$), Equation (7) defines the final demand for immunization in the arcs $d_{12} = 300$ and $d_{13} = 200$.

By incorporating the demand function in this way, demand becomes a property of the arc and not the node, as is typical in network optimization problems. In addition, Equations (7) and (8) remain applicable for any functional form – such as linear, exponential, or polynomial decay. Finally, functions that incorporate additional location or arc factors beyond distance could be defined and used. Thus, behavioral research regarding access to healthcare in a particular context can be easily incorporated in our formulation. See 4.2 for how we defined the demand function in The Gambia case study.

3.2.2 Outreach cost and capacity

In the exploratory model, the cost of an outreach operation added a fixed implementation cost with the cost of vaccinating each population center from the outreach site, which we fabricated by making more distant centers more expensive. Feedback from experts highlighted that cost and capacity of an outreach operation was not fixed but dependent on the distance to and resources supplied by the health centers. In addition, the immunization cost at an outreach site was not dependent on the distance from the outreach site to the population, as the population traveled to the outreach site. This patient travel does not impact cost but undoubtedly impacts the number of patients that access a facility, and thus the endogenous demand.

The authors updated the model formulation to incorporate this feedback adding a resource flow from the fixed health center f to the outreach site o. Resources included everything necessary to implement an outreach operation. Interviews with UNICEF experts identified five fundamental resources necessary to guarantee outreach implementation: (1) vaccines doses; (2) cold boxes and ice packs; (3) transport vehicle; (4) nurses responsible for administering vaccines; and (5) other basic equipment, such as needles.

The flow of resources along the network arc determined the cost and capacity for each outreach site. In defining parameters for this flow, it was helpful to create resource bundle concept, which is defined as a unitary package of the essential resources necessary to implement a certain amount of capacity for each outreach site. This enabled definition of cost and capacity drivers that could change according to location while ensuring that all required resources were accounted for.

The model restricted the amount of resource bundles that could be allocated to each operation to integer values. The resource bundle concept enabled customization of the mix of resources required or possible. For example, one vehicle could seat two people and hold 12 cold boxes while another could seat five people and hold five cold boxes. Thus, the formulation could be tailored to different contexts by defining a "recipe" of ratios for the five key resources in the bundle to the unitary resource. The definition of the unitary resource depends on the most relevant factor to in specific circumstances and/or the operational bottleneck. In one context, nurses could have open access to transportation. In this case, the unitary resource would be a single nurse, the modeler would derive a ratio for the resources each nurse, and the model would allocate nurses. In a different context, the limiting factor might be the number of available vehicles. Thus, the unitary resource would be a vehicle that is filled with a relative amount of other resources.

In The Gambia, the vehicle was often defined as the unitary resource for the bundle, though the flexibility in customizing resource flows for different contexts is important. With the unitary resource defined, it was necessary to define conversion factors that flow the relative amount of key resources per bundle. Conversion factors would depend on the specific characteristics of each country's immunization network logistics, such as vehicle types and cold box sizes. Table 2 summarizes the conversion factors necessary for a vehicle-driven bundle. These parameters are included in the formal model formulation as an example that is applicable for The Gambia.

3.2.3 Mathematical formulation

This section presents the mathematical formulation of the formal model. Our objective function remains the maximization of the

Table 2 Resource bundle parameters

Input variable	Unit
V_{cv}	Number of cold boxes per vehicle
Ve	Maximum number of employees per vehicle
V_{dc}	Number of doses per cold box
PE_o	Employee productivity in outreach operation [doses/day]

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total amount of doses distributed. The total amount of doses was obtained through the sum of the doses distributed from fixed health centers X_{fj} plus the ones from outreach sites X_{oj} (Equation 1). There were three key decisions in the formal model: (1) which facilities will serve each region; (2) doses supplied to each region; and (3) how many resource bundles will be sent from each health center to each outreach site. This third decision was an addition to the exploratory model formulation.

To model this new feature, we added a new variable to capture the flow of resource bundles from health centers to outreach locations: X_{fo} = resource bundles sent from fixed health center f to outreach location o. Thus, the decision to send bundles to an outreach site defined whether the candidate location was used or not. Table 2 introduced the parameters that define the bundle structure used in The Gambia case. The parameters that make up the cost of a resource bundle, Equation (9), were the vehicle cost per km, the distance, the number of employees in a vehicle, and the cost per employee.

Formal model formulation:

$$\text{Maximize} \sum_{j \in \mathcal{J}} \left(\sum_{f \in F} X_{fj} + \sum_{o \in O} X_{oj} \right) \tag{1}$$

S.T

$$\underbrace{\sum_{f \in F} \sum_{o \in O} X_{fo} \cdot C_{fo}}_{A} + \underbrace{\sum_{f \in F} \sum_{o \in O} Cv(X_{fj} + X_{oj})}_{B} + \underbrace{\sum_{j \in \mathcal{J}} \left(\sum_{f \in F} X_{fj} \cdot \frac{CE_f}{PE_f} + \sum_{o \in O} X_{oj} \cdot \frac{CE_o}{PE_o} \right)}_{C} \leq B \tag{2}$$

$$X_{fj} < d_{fj} \cdot Y_{fj} \quad \forall f \in F, \forall j \in \mathcal{J} \tag{3}$$

$$X_{oj} < d_{oj} \cdot Y_{oj} \quad \forall o \in O, \forall j \in \mathcal{J} \tag{4}$$

$$\sum_{f \epsilon F} X_{fo} \cdot Vp \geq \sum_{j \epsilon \mathcal{J}} X_{oj} \quad \forall o \in O \tag{5}$$

$$\left(\sum_{f \in F} Y_{fj} + \sum_{o \in O} Y_{oj} \right) \leq 1 \quad \forall j \in \mathcal{J} \tag{6}$$

$$d_{oj} = D_j \cdot \propto_{oj} \quad \forall f \in F, \forall j \in \mathcal{J} \tag{7}$$

$$d_{oj} = D_j \cdot \propto_{oj} \quad \forall o \in O, \forall j \in \mathcal{J} \tag{8}$$

$$C_{fo} = Cov \cdot Dist_{fo} + CE_o \quad \forall f \in F, \forall o \in O \tag{9}$$

The model includes several complex constraints that deserve further explanation. Equation (2) represents the budget constraint. To simplify its explanation the total cost was broken down into its three expressions: (A) the vehicle operation costs; (B) the vaccination cost at fixed health centers; and (C) the vaccination cost at outreach sites. The first cost component of the budget constraint refers to the cost of sending the resource bundles. The second is a straightforward calculation of the cost per dose multiplied by the number of doses. The last cost component calculates the direct labor costs for vaccination by multiplying the daily cost of an employee by the total amount of employees required to administer doses.

The resource bundle constraint, Equation (5), guarantees that the number of vaccines administered at each outreach site does not exceed the vaccines in each resource bundle. This is a generic constraint. Vp, the number of doses per bundle unit, will depend on how the resource bundle is defined. The resource bundle definition in Equation (5) is generic. It is possible to replace Equation (5) with distinct equations by resource to help decision-makers frame a more complex resource context. For example, in developing our case study we explored both a human resources constraint (Equation 10) and a vehicle capacity constraint (Equation 11).

$$\sum_{f \epsilon F} X_{fo} \cdot PE_o \cdot Ve \geq \sum_{j \epsilon \mathcal{J}} X_{oj} \quad \forall o \in O \tag{10}$$

$$\sum_{f \epsilon F} X_{fo} \cdot Vcv \cdot Vdc \geq \sum_{j \epsilon \mathcal{J}} X_{oj} \quad \forall o \in O \tag{11}$$

In the human resources constraint, Equation (10), each vehicle can carry a maximum Ve number of employees with average productivity of PE_o doses per day. Assuming each outreach trip must start and end on the same day, given the available employees in each vehicle, the number of doses per resource bundle cannot exceed PE_o * Ve doses per day. In terms of vaccine doses is given by Equation (10). A similar approach was taken with the vehicle capacity constraint, Equation (11), to calculate the maximum amount of vaccinations per outreach due to the vehicle transportation capacity of vaccine doses. In this case, each cold box has a maximum number of doses per unit, Vdc, and each vehicle has a maximum number of cold boxes it can fit, Vcv. Stakeholders from The Gambia ultimately decided that the resource bundle would be represented by the vehicle capacity for our case study, thus using Equation (11).

4. The Gambia case study

Application of the model to a real-world case study was a goal of this research. This section presents an overview of the current network structure in The Gambia and describes how the empirical data were gathered and transformed to be used in the model and how the endogenous demand functions was calibrated. Lastly, the findings are presented.

The Gambia's vaccine network followed a typical vaccination supply chain design: a national store, regional distribution centers, health centers, and outreach sites. The fixed facilities (regional stores, national stores, and health centers) were not only used for immunization services but were also part of other health supply chains. The flow of immunization commodities started at the ports and moved to the national store. Next, products were distributed to the seven regional stores and flowed down to health centers and outreach sites. Regional stores were supplied every quarter by trucks coming from the national stores. Each health center collected commodities at the regional stores every month, using an available vehicle. This vehicle was also used for outreach operations.

Outreach trips departed from the health centers, where medical staff left in a vehicle at the beginning of the day with all the necessary equipment, traveled to the predetermined outreach site, vaccinated, and returned the same day. A

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predetermined monthly schedule defined the specific days for the immunization service at each outreach site and health center.

Our model considered distribution in the vaccine network. Therefore, the focus was on defining the optimal distribution schedule to the outreach sites, the optimal location of outreach sites (i.e. which should be opened and closed), and the necessary personnel. The model did not suggest the opening or closure of existing fixed health centers. We next provide details for key elements of the network design problem.

4.1 Nodes

The nodes in the model were comprised of regions, health centers, and outreach sites. This section discusses how the regions' populations were derived, how potential outreach sites were selected, and how we calculated the distances between the nodes.

4.1.1 Regions

The UNICEF field office in The Gambia provided population by existing catchment areas as a data source. Without information on how UNICEF defined the catchment areas, the model could not utilize these data to inform demand for new catchment areas. Instead, the model incorporated the Socioeconomic Data and Application Center's 1-km population projections for 2020 (Jones *et al.*, 2020). Extracting a GeoTIFF from SEDAC, masking the extract for the geographic boundaries of The Gambia, and then creating point data for a 2-km grid resulted in 3,952 centroids each with a corresponding population, which were treated as regions in the model. While this dataset's estimated total population is 10% less than the dataset provided by UNICEF, the population was similarly geographically distributed.

4.1.2 Facilities: fixed health centers and outreach sites

UNICEF provided the geolocation of current health centers and outreach sites. Figure 2 shows the distribution of these sites. The calculation of distances between these sites was a key component of the model formulation as it impacts both the endogenous demand function and the outreach distribution costs. With network design problems, it is common to work with linear Euclidian distances instead of road distances. However, the road network distances and the calculated linear distance differ dramatically for some geographies. This is the case in The Gambia, as it is a long, narrow country divided by a large river. As a result, the linear distance between two points on opposite river banks differs significantly from the road distance.

For the case study, the distances between health centers and outreach sites utilized the shortest road distance, using Open Street Maps (OSM), while regions to outreach sites used a linear distance. The model used linear distances between the population regions to the facilities for two main reasons: many regions in the 2-km grid had no access to the road network, therefore the calculation of road distance was not possible; and we assume that rural areas will walk directly to a vaccination site rather than take the road.

The starting point for candidate locations for outreach sites was the 2-km grid, with 3,952 centroids, used to create the region nodes. Next, we identified the closest node in the OSM road network for each centroid. Lastly, only the 2,331 unique nodes in the road network were used as candidate sites in the model. Figure 3 shows how this approach dramatically reduced the number of candidate outreach sites in rural areas as the sparse road network resulted in additional overlapping closest nodes.

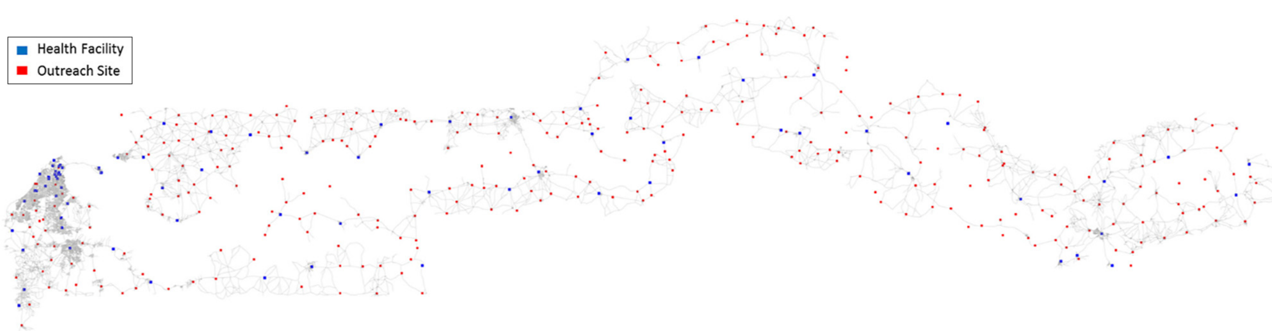
4.2 Endogenous demand function

Our literature review on the impact of distance to a facility on access levels did not reveal a definitive shape for the demand function. Typically, researchers chose linear decay with maximum distances up to 10 km. We defined the demand function as a piecewise linear decay function with two key parameters: the distance up to which 100% of the population access services, d_1, and the distance beyond which 0% access services, d_2.

$$\alpha_{fj} = f(\mathrm{Dist}_{fj}, d_1, d_2)\begin{cases} 1, & \text{if } \mathrm{Dist}_{fj} < d_1 \\ 1 - \dfrac{\mathrm{Dist}_{fj} - d_1}{d_2 - d_1}, & \text{if } d_1 \leq \mathrm{Dist}_{fj} \leq d_2 \\ 0, & \text{if } \mathrm{Dist}_{fj} > d_2 \end{cases}$$

Figure 3 Candidate outreach sites using 2-km grid and OSM road network

Figure 2 Baseline health centers and outreach sites



The same function was used for outreach sites to calculate α_{oj}. The low reach demand function ($d_1 = 0$, $d_2 = 2.5$) reflected Ibnouf *et al.* (2007), which suggested that usage of health facilities significantly drops after 30 min of walking (approximately 2.5 km). The moderate reach demand function ($d_1 = 1$, $d_2 = 5$) reflected (Feikin *et al.*, 2009) and also Blanford *et al.* (2012), which focused on one hour of walking. The high reach demand function ($d_1 = 2$, $d_2 = 10$) reflected other studies and input from UNICEF that vaccinations are valued in The Gambia such that people travel further than 5 km for services.

4.3 Outreach schedule

Each region could be served either by a fixed health center or by an outreach site. According to UNICEF interviews and data, Gambian immunization professionals work a fixed monthly schedule that specifies each day of the week where the team of each health center should work. The 2019 immunization schedule was used to derive how often a health center performed immunizations and how frequently an outreach site is visited and from which health center. After cleaning the schedule data, we analyzed the number of visits per month at health centers and outreach sites. The results are shown in Figures 4 and 5.

In both histograms there are bins with no scheduled immunizations. There are 19 health centers with no schedule in Figure 4. We assumed that these facilities did not have outreach treks originated from them, but they do provide immunizations services. In the baseline, we treat them as candidate locations to provide immunization services. In the second histogram, Figure 5, 42 outreach sites are found in the location data but not in the schedule data. In this situation, we assumed that these outreach sites were unused. UNICEF representatives supported this assumption saying that the schedule information was more reliable than the location data.

Figure 4 Number of scheduled visits per month

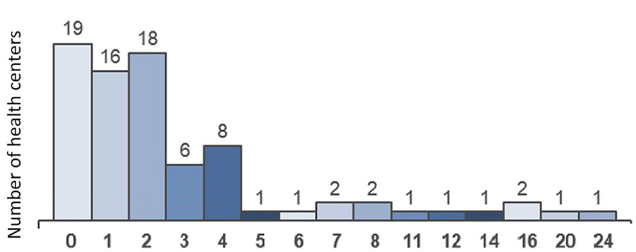
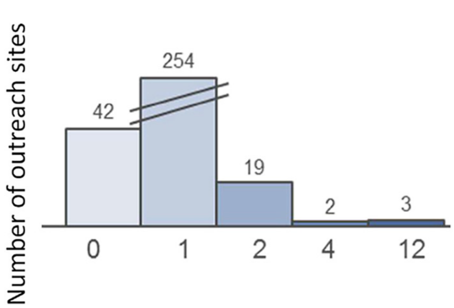


Figure 5 Number of visits per month (outreach sites)



Using data provided by UNICEF on the target population assigned to each facility, we determined that 5.07% of the target population is served from outreach sites with zero scheduled outreach visits. For this reason, we optimized the population allocation decision in the baseline and did not enforce the population allocation constraint.

4.4 Costs

The costs in the resource bundle were integral to the optimal solution. Based on interviews, we concluded that vehicles were the unitary resource in the bundle to provide vaccination services in The Gambia. Unfortunately, each health center had only one vehicle available for performing both collection from storage and outreach distribution. In addition, because each outreach trip took one day, vehicles were scarce resources that must be carefully planned.

The vehicles used in The Gambia network were Ford Everests, Nissan Patrols, or Toyota Land Cruisers (UNICEF, 2019). UNICEF's internal studies estimated that the average vehicle operating costs, Cov, for the mentioned vehicles averaged 0.6 \$/km. The same study concluded that 12 cold boxes could reasonably fit in the back of one of those vehicles. However, this transport capacity assumed the entire rear of the truck was filled with cold boxes. By considering the average vehicle size, box sizes, and the photos, we concluded that it was reasonable to assume that each vehicle was capable of taking a maximum of $Ve = 5$ people and $Vcv = 3$ cold boxes at the same time.

The productivity of nurses at outreach sites was affected by travel time and the time needed to set up at the outreach site. Based on the interviews with UNICEF, we concluded that it was reasonable to assume only six hours of the day were available to perform the vaccination services. Mokiou *et al.* (2018) outlined times involved in vaccinations leading us to estimate that 20 doses could be administered per hour. Therefore, using six hours instead of the health center nurses 8 h day, the average daily productivity of an employee at an outreach trip, PE_o, could be estimated as $20 * 6 = 120$ doses per day.

The cold box most commonly used in The Gambia was the Blowkings 7-L unit measuring 49 × 44 × 49 cm (UNICEF, 2019). To derive the capacity measured in the number of doses in a cold box, we determined the "packed volume" of each vaccine dose vial. We defined packed volume as the average volume occupied by a dose plus its package and surrounding space in the box. The packed volume of each dose was calculated by dividing the annual volume of vaccines (m^3) by the yearly doses administered. Based on this calculation, we concluded that each dose volume is 26.20 cm^3. Next, the number of doses per cold box, Vdc, was determined by dividing the cold box volume by the dose volume, resulting in 267 doses per cold box.

By combining the vehicle's transportation cold box capacity for the cold boxes, employee productivity, and the cold boxes' capacity, we calculated the capacity for doses per vehicle as:

1. Vaccination capacity per vehicle in terms of employee = 120 × 5 = 600 doses.
2. Vaccination capacity per vehicle in terms of cold boxes = 267 × 3 = 802 doses.

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The bottleneck for an outreach operation was not the capacity to transport the vaccines or the precise number of doses each cold box can hold but the number of employees. The constraining factor of an outreach operation was the number of nurses available and their productivity (see Table 3).

4.5 Optimization scenarios

Three different scenarios were developed to assess the model. The model baseline was defined by the first scenario running with the current facilities, existing outreach sites, and current site visit schedule. In the second scenario, the visit constraint was relaxed, but only existing outreach sites were considered. Finally, in the third scenario, both the outreach site locations and the visit schedule were optimized (see Table 4).

The optimized baseline was the scenario to which other scenarios were compared. The facility location, population, and outreach schedule data all matched the information described in earlier sections. The minimum budget necessary to service the bundles required by the outreach schedule was determined by varying the budget until the model became feasible. The optimization determined which regions were serviced by which nodes.

Table 3 Summary of input parameters

Input variable	Description	Value	Unit
C_{ov}	Vehicle operation cost	0.6	\$/km
C_V	Total cost to have a dose available at fixed health center	0.02	\$/dose
CE_o	Employee cost at fixed outreach site	3.68	\$/emp/day
CE_f	Employee cost at fixed health center *f*	3.68	\$/emp/day
PE_o	Daily employee productivity at outreach *o*	120	Doses/emp/day
PE_f	Daily employee productivity at health center *f*	160	Doses/emp/day
V_{cv}	Number of cold boxes per vehicle	3	Cold boxes
Ve	Maximum number of employees per vehicle	5	Nurses
V_{dc}	Number of doses per cold box	267	Doses

Table 4 Overview of optimization scenarios

	1. Optimized baseline	2. Outreach schedule optimization	3. Outreach schedule and location optimization
Population allocation	Optimized	Optimized	Optimized
Health center locations	Fixed	Fixed	Fixed
Outreach site locations	Current	Current	Optimized
Outreach allocation and schedule	Current	Optimized	Optimized

The outreach schedule optimization scenario determined if the current outreach sites could be utilized more efficiently. For the purpose of our model, efficiency was defined on whether it was possible to achieve better vaccine access levels without changing the current outreach footprint. The increase in operational efficiency was optimized through the following variables:

1. Number of bundles sent from a health center *f* to outreach site $o - X_{oj}$.
2. Which node, *f* or *o*, services each region - Y_{oj}, Y_{fj}.
3. Number of health centers open.
4. Number of outreach sites used.

The optimization results determined the number of vehicles necessary at each facility and the number of employees, suggesting a better allocation of existing resources.

The last scenario, in addition to the population allocation optimization (Scenario 1), and the schedule optimization (Scenario 2), also optimized the location of the outreach sites. All possible outreach site candidates were considered.

4.6 Results

The key results in the case considered solutions for the three optimization scenarios introduced in Table 4: optimized baseline; schedule and allocation optimization with current outreach sites; and the schedule and outreach site location optimization. More detailed analysis explored solution characteristics for The Gambia as a basis for managerial insights and recommendations that extend beyond the specific case.

4.6.1 Impact on coverage

First, we identified which demand function best matched The Gambia's current vaccination DTP3 rates, 93% in 2018 and 88% in 2019 (WHO, 2020). We considered each of the three demand functions, described in Section 4.2, using the optimized baseline scenario that assumes the current network structure. Generally, the vaccination coverage increased as the budget increases until it reaches a saturation point (see Figure 6) depending on the budget. The saturation point indicates the maximum population has been reached given the demand function and network design enabled by the budget. The high reach demand function ($d_1 = 2$, $d_2 = 10$) with a saturation coverage of 91.0% was the only one that approximated the empirical coverage data. This function aligned with input from UNICEF assuming that people value vaccinations and would be willing to travel those distances for immunization services. We conducted sensitivity analysis with the moderate reach demand function (see Section 4.7), but the maximum coverage for the low reach demand function was too low and unrealistic from stakeholder perspective to merit further consideration. The high reach saturation point also defined a budget level of \$12,000 where current levels of coverage could be expected. This monthly budget of \$12,000 was used as a reference point for our further analysis.

Second, we explored the impact of optimization scenario on coverage. Some benefit could be derived simply by improving the outreach allocation and schedule as, at the reference budget of \$12,000, the coverage increased from 91.0% to 92.8% (see Figure 7). Alternately, optimized allocation and schedules could also provide over 91% coverage with a lower budget of

Figure 6 Vaccination coverage by demand function and budget for the Optimized Baseline Scenario

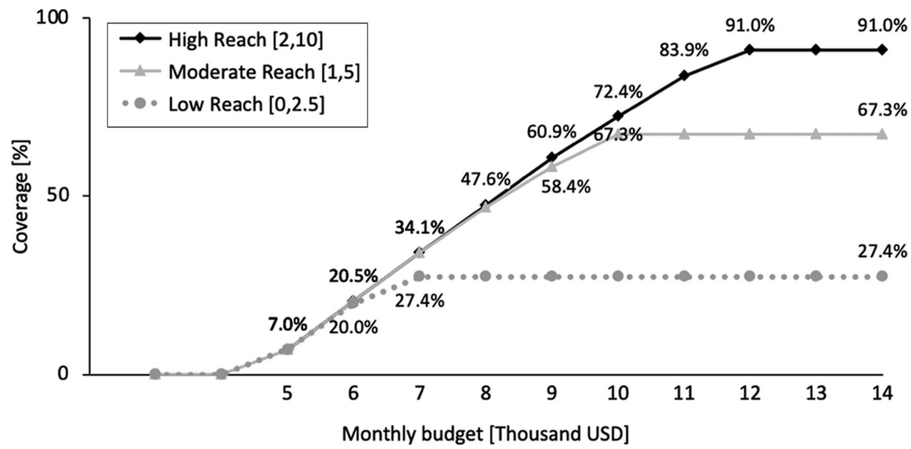
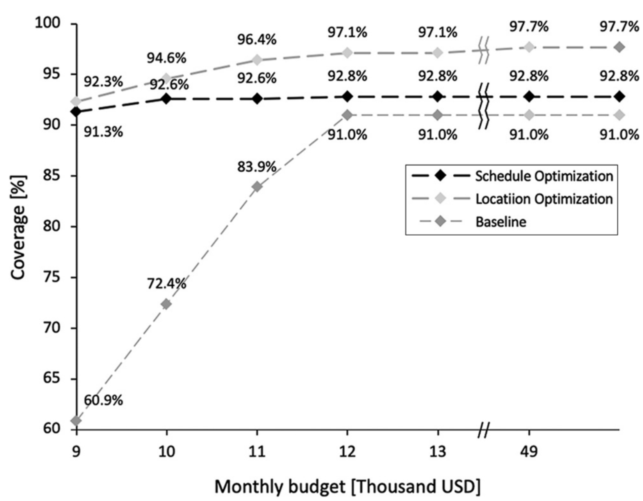


Figure 7 Comparison of vaccine coverage by optimization scenario with high reach demand function



$9,000. However, the biggest benefit came from optimizing the network locations. At the $12,000 reference budget, optimizing outreach sites and schedules together increased coverage to 97.1%. There were notable diminishing returns on coverage from further budget investment.

4.6.2 Solution characteristics

We then explored solution characteristics for each optimization scenario to build intuition. We did not seek to precisely calibrate coverage since, without further research on the nature of the demand function, this was impossible. However, with patient behavior assumptions that reasonably represented reality, the model could provide important insights on how network design decisions increase vaccination coverage. We focused further analysis on the scenario with high reach demand function and a monthly budget of $12,000 to consider metrics like the number of outreach sites, distance, asset utilization, and cost.

The baseline scenario used 263 current outreach sites. Vaccine coverage increased by 1.8% in the schedule optimization scenario because 311 outreach sites were used, indicating that there were inefficiencies in the baseline. When the network structure was optimized to select outreach sites, the total number of outreach sites increased 44% to use 449 of the 2,331 possible candidate sites. Figure 8 offers a map of the overall solution and Figure 9 provides a detailed zoom of an area that shows how outreach site expansion can improve proximity to services.

Compared with the baseline scenario, schedule optimization reduced the average distance from fixed health center to outreach site by 57%, from 21 km to 9 km. With more candidate outreach sites, the location optimization further reduced the average distance by another 11% to 8 km and

Figure 8 Optimized network - 73 health centers (blue) and 449 outreach sites (red)

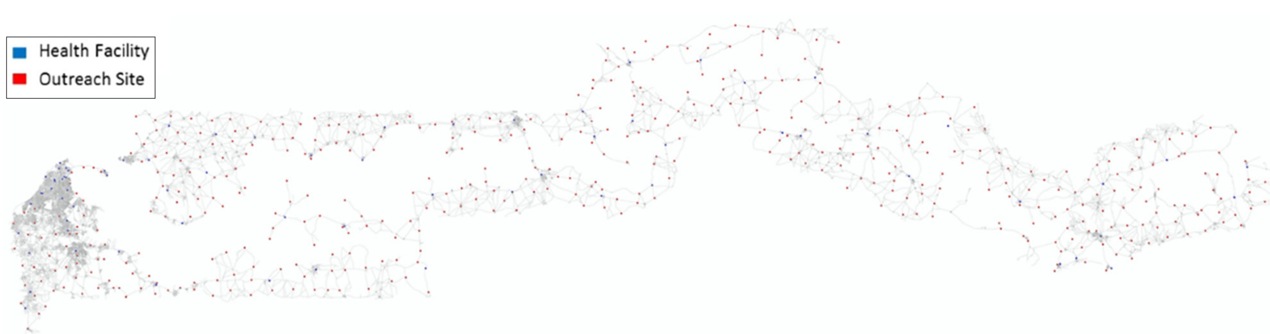
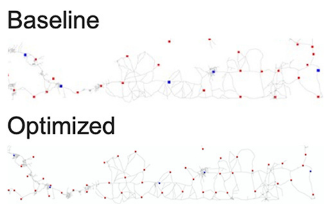


Figure 9 Detail of baseline and optimized network maps



increased the vehicle utilization. Compared with the baseline, location optimization used 33% more health centers for outreach (from 46 to 61) and sent 69% more trips per health center (3.6 per month for the baseline, 6.1 per month for location optimization). We noted that no health centers had over 20 trips per month, meaning the outreach plan was feasible even if a health center only had one vehicle. It is also important to note that monthly variable vehicle cost for vaccination service could actually decrease as the reduction in average distance more than offsets the increase in trips (approximately 75 km/month for the baseline and 49 km/month for location optimization).

Better operational efficiency lowered cost. Schedule optimization reduced the cost to serve from outreach sites by 8%, from $0.112 per dose to $0.103, compared to the baseline. Location optimization further reduced the cost to serve from outreach sites by 16% to $0.87. The cost to serve from fixed health centers was $0.043 per dose across the scenarios.

With no vehicle costs and more productive employee days, the cost to serve was lower in a fixed health center. Therefore, it could be expected that a region served by a fixed health center in the baseline would continue to be served similarly in the optimized scenario. This would be true if demand was a fixed property of the node and did not vary with patient proximity. However, as new outreach locations open, populations may now have a closer location to visit. Compared with the baseline scenario, schedule optimization had a 17% increase in the doses delivered by outreach sites and a 11% decrease in service by health center. Location optimization resulted in a further 29% increase outreach site volume and a 23% decrease at health centers.

Based on the total amount of vaccines administrated in the health centers, it is also possible to calculate the employees-day required in each health center to fulfill its onsite demand, i.e. this calculation does not include employee requirements for the outreach sites. Overall, the average number of employees-day in the baseline is 7.3 while in the optimized solution is 4.3.

4.7 Sensitivity analysis

In addition to the default scenario discussed in depth above, we ran sensitivity analysis on three key assumptions. First, we explored application of the moderate reach demand function ($d_1 = 1$, $d_2 = 5$). Though the baseline with this demand function did not align best with empirical coverage in The Gambia, see Section 4.6.1, it is important to demonstrate how a configurable demand function enables sensitivity analysis. In addition, exploring a different demand function can build intuition on the how network structure might change in an area with lower outreach potential, which might be the case in other countries. With a monthly budget of $10,000, where the baseline scenario reached a saturation point with 67.3% coverage for this demand function, location optimization enabled coverage of 81.8% (see Figure 10). Doubling the monthly budget to $20,000 bumped coverage to 89.3%. Coverage increases came through more aggressive outreach expansion for this demand function, resulting in fewer fixed health centers and 1,469 outreach sites (see Figure 11). In regions where patient reach is more challenging, health authorities must be prepared to consider a shift from traditional health centers a more aggressive community-based vaccination network.

Second, we consider the sensitivity of network design to transportation costs. Higher transportation costs effectively decrease the budget, but with an implicit tradeoff in network design. The optimization model weighed the value of budget savings from avoiding distant outreach locations with the loss of outreach in those areas. Doubling the transportation cost, from $0.6/km to $1.2/km, reduced the coverage from 94.6% to 92.5% in the $10,000 budget scenario and from 97.1% to 95.8% in the $12,000 budget scenario (see Figure 12). On the other hand, lower transportation cost implicitly explores opportunities to deploy budget savings in the network by opening additional outreach centers resulting in improved vaccination coverage, though with diminishing returns using the $12,000 budget. Figure 13 shows changes in the number of sites, which is the key driver in coverage changes.

Finally, we consider sensitivity analysis on the cost per dose. Emerging pathogens that result in a pandemic could require newly developed vaccines that are more expensive, which has been the case with Covid-19. Like transportation cost, vaccine procurement cost changes shift the available budget but without any implicit network design tradeoff. By doubling the cost of a dose of vaccine, the vaccine coverage dropped from 97.1% to 91.8% (see Figure 12). Figure 14 supports that finding as higher vaccine acquisition cost reduced the available budget, resulting in fewer outreach centers. Analysis like this could be critical in helping international aid organizations determine the support required by LMICs in procuring emergent vaccines. Given constrained national budgets, higher procurement costs could dramatically reduce access to this vital public health intervention.

Figure 10 Vaccine reach by monthly budget for moderate reach demand function in the location optimization scenario

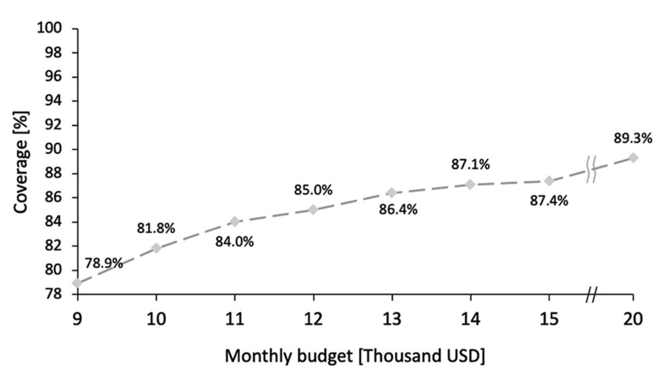


Figure 11 Number of facilities by monthly budget for moderate reach demand function

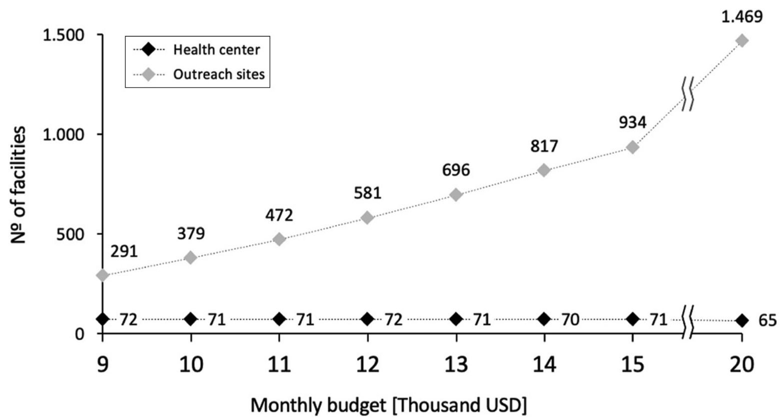


Figure 12 Sensitivity analysis of transportation and vaccine cost

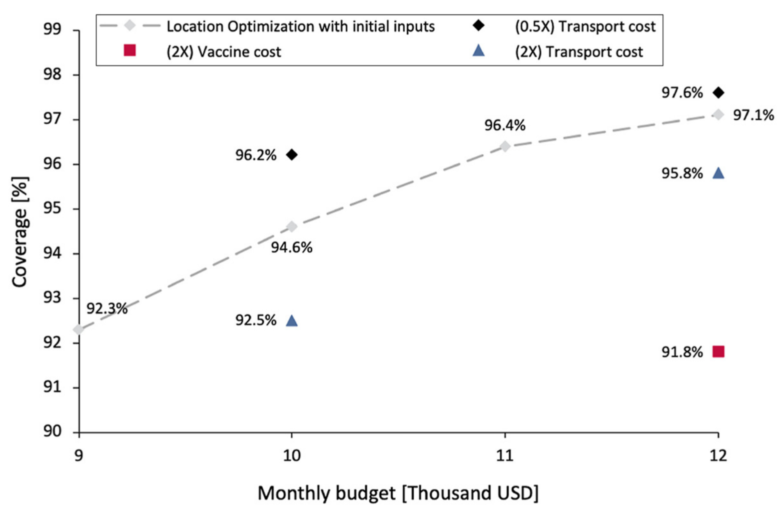
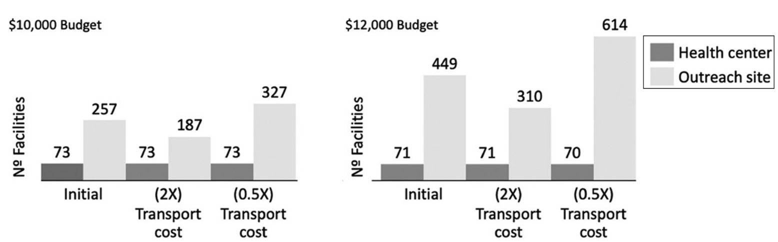


Figure 13 Sensitivity analysis of transportation cost at $10,000 and $12,000 monthly budgets

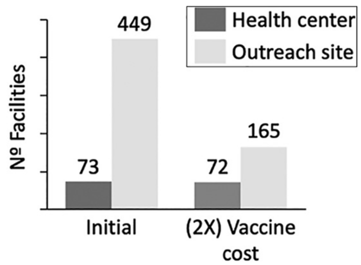


5. Discussion

This research sought to answer the primary research question of how to design vaccine networks in order to maximize immunization coverage given the tight budgets that are common in LMICs. The MIP formulation with an endogenous demand function linking coverage with proximity designed the vaccine network around the principle of convenience for community members to access immunization services. Detailed modeling of specific commodities, equipment, assets, and skilled workers revealed resource scheduling improvements that can increase coverage in The Gambia from 91.0% to 92.8% using the existing network of 80 health centers and 311 outreach sites. Further, by reallocating the budget to open an additional 138 outreach sites from among 2,020 candidate locations, the immunization coverage increased to 97.1%.

These results demonstrated the impact of important contributions to the literature. One model aspect that was important to UNICEF stakeholders but not common in the

Figure 14 Sensitivity analysis of vaccine cost for $12,000 monthly budget



literature was defining the objective function to maximize immunization coverage subject to different budget levels to understand tradeoffs. The model provided original contributions to the literature on vaccine network design in two important ways that are generalizable and that reflect important contextual factors and empirical research in modeling activities.

First, endogenous calculation of demand as a function of distance to health facility location enables the model to effectively design the vaccine network around convenience to the community. Unlike prior efforts to incorporate distance as an endogenous causal factor for demand in maximizing coverage (Lim *et al.*, 2016), our model incorporates a general demand function that can reflect empirical health data. Unfortunately, extensive review of the literature did not reveal a robust demand function to causally link proximity of population to vaccination services with immunization coverage. For the case study, we calibrated a demand function that is commonly used in health literature with empirical coverage data for our focus country. Importantly, we developed the capability to conduct sensitivity analysis with a flexible demand function that could incorporate emerging evidence and/or expert insights on the link between proximity and coverage. Additional research is needed to determine the proper shape of vaccination demand functions.

Second, definition of resource bundles enabled us to incorporate various contextual factors to appropriately model requirements and costs for specific resources. Vehicles, which are scarce resources, emerged as the unitary resource to frame the bundle. The remaining physical and human resources in the bundle – vaccines, cold boxes, ice packs, other immunization supplies such as syringes and safety boxes, and skilled workers – could then be sized according to the expected demand for the outreach trip. Resource bundles enabled more accurate accounting of fixed and variable costs for both fixed health centers and outreach sites. They also enabled more precise resource deployment in defining flexible capacity by the number of employees or working hours and to optimize monthly schedules around key assets such as vehicles.

Results also reflect better model accuracy and credibility by embracing empirical research such as consultation with health system experts in the country and analysis of historical operations (e.g. outreach site schedules). Early use of a simple, exploratory model was very helpful in eliciting important contextual factors from experts at UNICEF and in the public health system. The Gambia case study also demonstrated effective data collection and analysis methods to estimate key parameters.

Sophisticated geospatial modeling also contributed to model accuracy and robustness by leveraging demographic and geographic data. Precise geographic distribution of population is essential in modeling the effect of proximity on community adoption. Extracting a GeoTIFF from the SEDAC 1-km population projections for 2020, masking the extract for the geographic boundaries of The Gambia and aggregating into a 2-km grid resulted in 3,952 centroids with a corresponding population to accurately capture dispersion. The list of possible outreach sites was created by using any nodes in the OSM road network within 2 km of these centroids, yielding 2,331 nodes that reflect the density of road networks in urban areas while dramatically reducing the number of candidate outreach sites on the sparse road networks in rural areas. This approach positioned outreach opportunities in more practical locations than Euclidean distance, which is more common in the literature.

While model development would be ideal, our exploration of various solutions also led to some managerial insights that could frame operations principles for countries that are not able to develop more sophisticated models. Many of these insights focus on more effective use of scarce resources:

1 Fixed health centers can and should use their current vehicle more to support more vaccine outreach. Compared with the baseline, location optimization used 33% more health centers for outreach and sent 69% more trips per health center. Vehicles assigned to health centers should be able to support this task, since the average number of trips per month was between 6–7, with the maximum being 20. If other vehicle requirements, such as collecting commodities at the regional stores, do not enable the 6–7 days per month for vaccination services, then regional store delivery approaches for commodity replenishment should be considered. Finally, the increase in outreach requirements would still enable vehicles to be shared between two health centers where needed. It is important to note that variable vehicle costs, such as fuel, for vaccination service could actually decrease as the reduction in average distance more than offsets the increase in trips.

2 Outreach trips vehicles often do not need to travel with full nurse capacity. While UNICEF did not provide data on the number of nurses sent on each outreach trip, we showed that the optimal number can be far from the total vehicle capacity. Therefore, the number of nurses should not be set by the vehicle size but rather be sized to the outreach campaign, as possible. Of course, this depends on a better ability to assess demand for an outreach site and health centers may be cautions in sending more nurses. If so, then excess nurse time in the outreach community could be used to improve vaccine outreach through complementary interventions. Activities could include vaccine information dissemination, data collection regarding convenience of services and beneficiary choices, and community engagement to address vaccine hesitancy by building trust. As an accurate demand function remains one of the fundamental aspects for improving evidence-driven vaccine distribution strategies, robust documentation of nurse experiences in the community would be valuable

empirical data to further shape model and policy development.

3 Increasing coverage requires more outreach sites but also reduces volume at fixed health centers, which could be used for other health services. The opening of outreach sites to reach populations will also reduce service in fixed health centers, i.e. people shift service from health center to outreach site. In The Gambia case, the number of doses provided via health centers decreased by 23% for some scenarios. Sensitivity analysis with the moderate reach demand function showed that in regions where patient reach is more challenging, the shift from traditional health centers to a community-based vaccination network would be even more aggressive. Health leaders should not be alarmed by a drop in vaccinations at traditional health centers but instead see the reduced vaccination volume as an opportunity to utilize the fixed facility for other important health services.

4 Gains can be made without sophisticated tools by managing outreach allocation and scheduling more actively. Vaccine coverage increased by 1.8% with allocation and schedule improvements alone, in part because the current schedule only used 82% of the outreach sites listed in the master file. Tactical resource decisions must continually adapt to contextual conditions, even if sophisticated GIS and optimization software solutions are occasionally implemented, to maintain effective utilization of scarce resources. Continual alignment of outreach site volumes and visit frequency with demand is important regardless of the application of sophisticated tools.

6. Conclusion

This paper defined a novel model to design vaccine networks by optimizing facility location and resource deployment in order to increase immunization coverage within the resource constraints of LMICs. Results from a case study in The Gambia showed that by opening new outreach sites and optimizing resource allocation and scheduling, the Ministry of Health could increase immunization access from 91.0 to 97.1% with the same budget. Considering specific solutions for The Gambia framed more generic operations principles for countries that are not able to develop sophisticated models.

The research contributed to the study of vaccine network design in two ways. First, endogenous calculation of demand as a function of distance to health facility location enabled the model to effectively design the vaccine network around convenience to the community. Second, the model's resource bundle concept more accurately and flexibly represented complex requirements and costs for specific resources, which facilitated buy-in from stakeholders responsible for managing health budgets.

As an accurate demand function remains one of the fundamental aspects for improving evidence-driven vaccine distribution strategies, robust documentation of nurse experiences in the community would be valuable empirical data to further shape health budget deployment for vaccine coverage.

This research was motivated to provide practical tools and insights such that LMICs could more easily pursue evidence-driven improvements to vaccine distribution in various contexts. Modeling efforts drew from empirical research and spatial analysis of publicly available demographic and geographic data to accurately define parameters and effectively represent important contextual factors. The model and the empirical research methods are general and can easily extend to other LMICs in order to improve coverage for routine immunizations. Managerial insights drawn from case study solutions are the foundation for gains in vaccine coverage even without application of sophisticated tools. Principles guide more effective utilization of common public health resources such as fixed health centers, vehicles, and nurses to extend vaccine outreach within existing budgets. Furthermore, the approach of extending outreach to communities with low vaccine coverage is not limited to LMICs. The global pandemic of COVID-19 has forced every country to consider how it can reach vulnerable communities with extended outreach services to improve vaccination uptake.

Future research should seek to leverage empirical data from COVID-19 vaccination drives, among other ongoing vaccination campaigns, to better understand the role of service proximity and other factors on vaccine adoption. Since the shape of the demand function has a strong impact on the model's results, research that provides evidence linking coverage and proximity would strengthen the impact of these network design methods.

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