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How to optimally prioritize the delivery of procurement orders for multiple vaccines when distribution capacity is interrupted.

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Declaro, bajo mi responsabilidad, que el Proyecto presentado con el título

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PRIORIZACIÓN DEL ENVIO DE ÒRDENES DE COMPRA DE MÚLTIPLES VACUNAS CUANDO LA CAPACIDAD DE DISTRIBUCIÓN SE HA REDUCIDO DRÁSTICAMENTE

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RESUMEN DEL PROYECTO

Introducción

Las vacunas son uno de los avances que más han contribuido al desarrollo de la sociedad en el último siglo. Son responsables de que múltiples enfermedades como la tuberculosis, que antes causaban miles de muertes, hoy haya sido virtualmente erradicadas en gran cantidad de países. A pesar de ello, cada año UNICEF estima que 1.5 millones de personas mueren por enfermedades erradicables por vacunas y casi 20 millones de niños no son vacunados [1].

La principal razón que impide el aumento de las tasas de vacunación en múltiples países en vías de desarrollo, después del factor económico, es la cadena de suministros. Múltiples investigaciones [2] [3] han denunciado la precariedad del sistema de distribución de vacunas en estos países en vías de desarrollo. Las cadenas de suministros para estos países tienen dos grandes debilidades. Primero, fueron diseñadas durante los años setenta [4] , lo que las hace anticuadas y poco óptimas para las necesidades actuales. Segundo, el volumen de vacunas que tienen que distribuir se ha incrementado considerablemente debido al aumento de la población y al aumento del número de vacunas en los planes rutinarios de vacunación. Estas características hacen que las cadenas de suministro para vacunas en países en vías de desarrollo sean muy débiles ante disrupciones como la sufrida en el 2020 por la pandemia de la COVID-19.

La pandemia afectó la cadena de suministro en países en vías de desarrollo en tres áreas. Primero, los gobiernos pausaron las campañas de vacunación rutinaria para prevenir contagios por la COVID-19, lo que generó la necesidad de almacenamiento de dichas vacunas, ya que no fueron administradas. Segundo, la vacuna para la COVID-19 se añadió, aumentando el volumen de vacunas a distribuir [5]. Por último, dos tercios de los aviones de pasajeros internacionales no volaron durante la pandemia [6], reduciendo considerablemente la distribución internacional de vacunas. Este proyecto de investigación se va a centrar exclusivamente en este último punto. En concreto, se quiere responder a la pregunta: Cómo priorizar el envío de distintas órdenes de compra de múltiples vacunas cuando la capacidad de distribución se ha reducido drásticamente es la cuestión que se pretende abordar en este trabajo desde el punto de vista del sistema de distribución de vacunas organizado por UNICEF.

El mercado de vacunas, especialmente para países en vías de desarrollo, presenta una serie de limitaciones; por un lado, los países no cuentan con grandes presupuestos, y por otro lado, el negocio de la manufactura de vacunas no es muy rentable, ya que opera con márgenes de beneficios muy restringidos. Las vacunas son muy costosas de producir debido a sus largos ciclos de producción. Además, tienen una vida útil muy limitada y han de almacenarse en cámara frigorífico. Esto hace que el precio de vacunas sea considerablemente alto y que la producción de vacunas sea bajo demanda, es decir, no hay exceso de producción.

Con el objetivo de hacer el mercado de vacunas más eficiente, entidades como UNICEF y PAHO empezaron a funcionar como agencias de compras. Estas agencias agrupan las órdenes de los países que representan y realizan una oferta pública. Debido a las economías de escala, la reputación de estas agencias y otras facilidades que estas agencias prestan a los fabricantes de vacunas, se produce una reducción del precio de las vacunas [7]. En el caso de UNICEF, su papel va más allá. UNICEF también se encarga del envío internacional de las órdenes de compra desde el fabricante a los países de destino. En situaciones normales, sin disrupciones en la capacidad de distribución internacional, UNICEF tiene la capacidad de distribuir todas las órdenes. El problema que esta investigación quiere abordar son las situaciones donde debido a una disrupción en la cadena de distribución global, UNICEF no puede enviar todas las órdenes. En esas ocasiones UNICEF ha de priorizar ciertas órdenes. La hipótesis en la que esta investigación está fundada es que aplicando técnicas de investigación operativa se puede desarrollar un modelo matemático que facilite la priorización y distribución de las órdenes, maximizando el uso de la limitada capacidad de distribución.

Estado de la técnica

Para abordar el problema primero se realizó una revisión literaria. Primero se centró en entender los factores que afectan las tasas de vacunación y los factores que afectan la expansión de enfermedades infecciosas. Se tomó como referencia el trabajo de [8] y [9] respectivamente. En segundo lugar, se centró en estudiar el estado del arte a la hora de abordar disrupciones en el sector de los vuelos comerciales. Para ello se estudio la recopilación de [10].

Metodología

El resultado de la investigación es la propuesta de un modelo de toma de decisiones desarrollado en dos etapas. En la primera etapa se cuantifican, entre otros, los factores que afectan a las tasas de vacunación, el estado de la cadena de distribución de los países considerados y una serie de factores que afectan la usabilidad de las vacunas. Mediante la técnica Proceso analítico jerárquico se sintetizan todos esos factores en el concepto de “Valor”, entendible como la recompensa que se obtendría por satisfacer una dosis de una determinada orden.

La segunda etapa consiste en un modelo de programación lineal. Teniendo en cuenta la capacidad de distribución disponible, el “Valor” obtenido de la anterior etapa y las órdenes a enviar, se computa el número de vacunas de cada orden que se tiene que enviar y a que ruta de entre todos los vuelos disponibles se ha de asignar. Esta asignación se realiza maximizando el “Valor” de las órdenes.

Resultados

Para validar el modelo, se ejecutó un pequeño estudio de Montecarlo, considerando un plan de envío de 45 órdenes, provenientes de considerar 3 vacunas distintas para los 15 países con peor porcentaje de vacunación según UNICEF, para el año 2020. Este año fue seleccionado debido a que por la pandemia COVID-19 la capacidad de distribución se redujo drásticamente a partir de marzo de ese año.

Las fuentes de datos usadas en el caso de estudio fueron principalmente UNICEF, WHO y el Banco Mundial. Respecto a la capacidad y el coste de distribución fue generada sintéticamente, al no disponerse de datos públicos. En total se hicieron 600 simulaciones donde el mes en las que cada orden tendría que ser recibida fue aleatorizado.

La solución propuesta se comparó con un modelo base, obteniendo una mejora de 158% en términos de “Valor” y una reducción de la demanda no satisfecha del 12%. Estas mejoras se produjeron a las expensas de un aumento de costes del 163%. Esta evidente limitación en el resultado genera la necesidad de realizar una revisión del modelo propuesto, en la que se solvente la posibilidad de exceder el presupuesto en distribución manteniendo la maximización del “Valor”.

Conclusiones

En conclusión, el resultado de esta investigación es un modelo de dos etapas en la que los responsables de distribución de UNICEF se podrían apoyar para tomar decisiones sobre la priorización de ordenes de vacunas en momento de limitada capacidad de distribución. Tras el buen desempeño del modelo en el caso de estudio, el siguiente paso para la verificación de este modelo sería el testeo con datos reales. Aunque el modelo todavía se encuentra lejos de ser aplicable, pensamos que esta investigación puede servir como semilla para el desarrollo a futuro de modelos basados en la estructura propuesta. Esta estructura se podría aplicar a otras industrias donde la reducida capacidad de distribución ponga a los técnicos en la tesitura de priorizar las ordenes de ciertos clientes.

Por último, esta investigación contribuye a los Objetivos de Desarrollo Sostenible (ODS) desarrollados por Naciones Unidas [11]. En concreto, los ODS 3, 10 y 17.

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HOW TO OPTIMALLY PRIORITIZE THE DELIVERY OF PROCUREMENT ORDERS FOR MULTIPLE VACCINES WHEN DISTRIBUTION CAPACITY IS INTERRUPTED.

Introduction:

Vaccines are one of the leading technological advantages of the 20th century. They are responsible for virtually eradicating diseases that killed thousands of persons in the past. Despite that, UNICEF reports that vaccine-preventable diseases cause 1.5 million deaths yearly and 19.4 million children miss out on vaccination yearly [1].

The main reasons stopping the increment of vaccine coverage are the lack of financial support and the national supply chain in low-income and low-middle-income countries (LIC, LMIC). Multiple articles warm that national supply chains in LIC and LMIC are unreliable under disruptions [2] [3]. The authors highlight two limitations. Firstly, supply chains were mainly designed around 1970, making them outdated [4]. Secondly, the volume of vaccines distributed is increasing due to the introduction of more antigens in routine vaccination plans and the population increment. This makes the national supply chain for LIC and LMIC weak against disruptions such as the COVID-19 pandemic of 2020 or the Russian-Ukraine conflict.

The COVID-19 pandemic affected the vaccine supply chain in three core areas. Firstly, the government stopped routine distribution campaigns to reduce their population's exposure to COVID-19. This led to the storage and, in some cases, expiration's of the vaccines that should have been distributed. Secondly, the COVID-19 vaccine was introduced in the distribution channels, increasing the number of vaccines to distribute, store and manage [5]. Lastly, two-thirds of the world's passenger jets were grounded [6], reducing considerably the international shipping capacity for vaccines. This research aims to reduce the disruptions caused by this last point, answering the research question: how to optimally prioritize the delivery of procurement orders for multiple vaccines when distribution capacity is interrupted. This question will be answered from the perspective of the vaccine distribution system managed by UNICEF.

The vaccine market, especially for LIC and LMIC, is limited by the government's lack of resources and the low profitability of vaccine manufacturing. Vaccines are costly to produce due to long production cycles, short life spans, and the necessity of cold storage. For this reason, there is no excess production and therefore increasing its price. Procurement agencies such as PAHO or UNICEF were developed to lower prices and make the vaccine market more efficient. These agencies grouped procurement orders from multiple vaccines and host tender offers. Due to the economies of scale, the reputation of these agencies, and other benefits that these agencies give manufacturers, vaccine prices are reduced considerably. In the case of UNICEF, it is also in charge of shipping vaccines from manufacturers to the countries. In typical situations, UNICEF can fulfill all the orders without any issue. The problem this research aims to solve is the situations when the distribution capacity is reduced drastically, and UNICEF cannot distribute all the procurement orders. In those situations, UNICEF must determine which orders to fulfill or not fulfill.

The hypothesis upon which this research project is founded is that operations research techniques could be applied to develop a decision-making model. The goal of this model is the prioritization and allocation of the procurement orders, maximizing the usage of the limited distribution capacity.

Literature review

To tackle the problem, relevant literature was reviewed. Firstly, it focused on understanding the main drivers of vaccine coverage and the spread of infectious diseases. The work of [8] y [9] was taken as the main reference. Secondly, the state-of-the-art used to handle airline industry disruptions was studied [10].

Methodology

The proposed solution for the research question is a two-stage decision-making model. The first stage synthesizes the drivers of vaccine coverage, the spread of diseases, and other factors relevant to the effectiveness of vaccines. The outcome will be the ”Value” earned for fulfilling each procurement order. It can be interpreted as the reward gained by fulfilling a dose of a given procurement order.

The second stage is a linear programming routing model. Considering the ”Value” from the previous stage, the available distribution capacity, and other factors, this stage is responsible for assigning the vaccines that should be shipped on a given flight and which ones are not worth shipping. The model will maximize value and will try to fulfill all possible orders.

Case Study

The proposed solution was tested with a Montecarlo simulation. Forty-five procurement orders from 3 vaccines and 15 countries with the lowest percentage of vaccination were routed for the year 2020. Due to COVID-19, the distribution capacity was reduced drastically from March of that year. The data used in the case study was sourced from UNICEF, WHO, and the World Bank. The distribution cost and capacity were not publicly available, and it was generated synthetically. In total, 600 simulations were executed. In each of them, the month that the procurement orders were scheduled to be received was assigned randomly.

The proposed solution was compared against a base case. The results were an improvement of 158 % in terms of ”Value,” and a reduction of not fulfilled demand of 12%. The downside was an improvement in the cost of 163%. Currently an improved model that limits the total cost is being tested.

Conclusions

In conclusion, the result of the research is a two-stage model that decision-makers at UNICEF could use to facilitate the prioritization of procurement orders when the distribution capacity is limited. Despite the good results of the solution, the model is in the early stage of development. Further studies should be made to test its behavior with real-world data. This research has two main contributions. Firstly the two-stage framework could be applied to industries others than the vaccine industry. Specially in situations where there is a sudden reduction of the distribution capacity, and the prioritization of the orders considers multiples criteria. Secondly, this research contribute to the achievement of the United Nations Sustainable Development Goals [11], specially goal 3: Good Health and Well-being; goal 10: Reduced Inequality and lastly SDG 17: Partnerships to achieve the Goal.

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To Sara González Torre.

"The proper function of man is to live, not to exist. I shall not waste my days in trying to prolong them. I shall use my time."
JACK LONDON

Contents

1 Introduction **1**

1.1 Introduction 1

2 Literature Review **5**

2.1 Usability of vaccines & spread of diseases 5

2.2 Disruption handling at the ISC 7

3 Methodology **9**

3.1 Approach 9

3.2 Procurement order prioritization model: 9

3.2.1 AHP 9

3.2.2 Criterias and subcriterias: 10

3.2.3 Evaluation of Criteria & alternatives: 12

3.3 Re-routing model: 13

3.3.1 Mathematical model: 14

3.3.2 Limitations: 17

4 Case study **19**

4.1 Problem Description 19

4.2 Problem Data 22

4.2.1 Procurement order prioritization model 22

4.2.2 Vaccine supply 23

4.2.3 Demand and Shipping capacity 23

4.2.4 Other considerations 24

4.3 Results 24

4.3.1 Model verification 24

4.3.2 Outcome 28

5 Discussion & Conclutions **31**

5.1 Futer work and discussion: 31

5.2 Conclution 32

Bibliography **33**

Appendix **35**

A Distribution capacity data generatior **37**

B Base line model **39**
B.0.1 Mathematical model: 39

C AHP algotithm **43**
C.1 Comparation Matrix & Weight Computation 43
C.2 Implemantation 44
C.2.1 Alogrithm 44
C.2.2 Auxiliary functions 44

D Randomly monthly allocation **47**

E Sustainable Development Goals **49**

List of Figures

1.1 Comparison of annual morbidity in 20th Century and current cases of vaccine-preventable diseases in the U.S. (Orensteina and Ahmedb (2017)). 2
1.2 Population growth (annual %) (World Bank (2019)). 3

2.1 Conceptual framework for vaccine coverage (David E. Phillips, Dieleman, Lim, and Shearer (2017)): 6

3.1 Full model flowchart. 10
3.2 AHP criterias and subcriterias for PO ranking in LIC and MLIC. . . 11
3.3 Pairwise matrix (PM) example. 13

4.1 Full model flowchart. 20
4.2 Reduction of international seats of the period 2019 vs 2020. 24
4.3 Routes: model BaseLine. (from: yellow, to: purple). 25
4.4 Manufactures(blue) and consumers countries (red) location. 25
4.5 Accumulated missing net demand. 26
4.6 "Value" of the fulfilled demand. 26
4.7 Fulfilled demand. 27
4.8 KPI: AMD 29
4.9 KPI: AMS 29
4.10 KPI: cost 30
4.11 KPI: Value 30

List of Tables

4.1 Model configurations 1. 21
4.2 Model configurations 2. 21
4.3 Aggregated results after outliers elimination. 28
4.4 MaxValue improvement over MinMax 28

Listings

C.1 AHPweight() 44
C.2 Rank() 45
D.1 Randomly order allocation 47

Acrónimos

ICAI	Insitituto Católico de Artes e Industrias
RIT	Rochester Institute of Tecnology
TFG	Trabajo Fin de Grado
SDG	UN Sustainable Development Goals
AHP	Analytical Hierarchy Process
ISC	Immunization Supply Chain
PO	Procurement Orders
LIC	Low Income Country
LMIC	Lower Middle Income Country
KS	Kolmogorov Smirnov
OR	Operations Research
OF	Objective Function
KPI	Key Performance Indicators

Chapter 1

Introduction

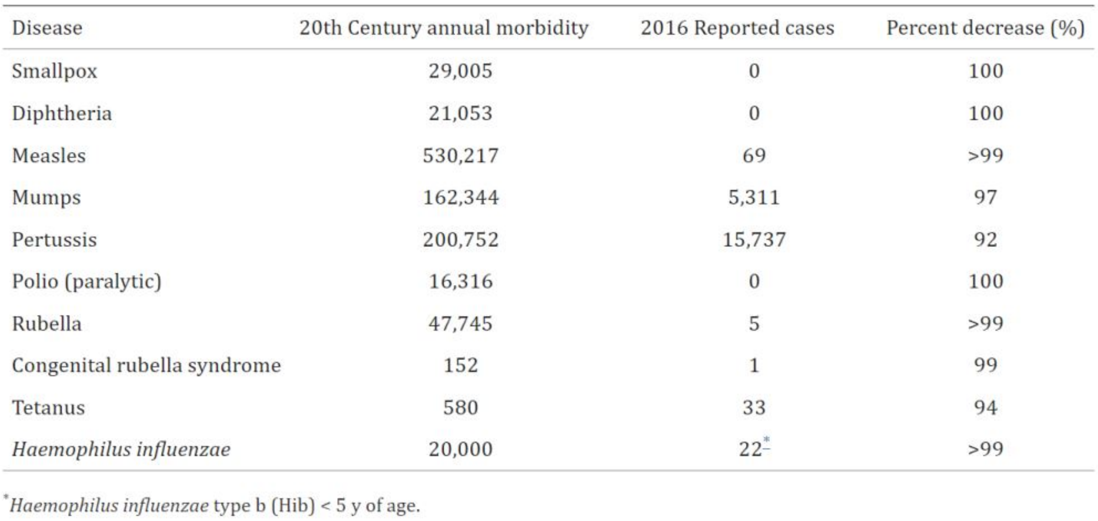
1.1 Introduction

According to the World Health Organization WHO (2019), immunization programs are credited for preventing 4.5 million deaths every year and are one of the most significant advances in modern medicine. Immunization is the most cost-effective mechanism against infectious diseases. They have the advantage of preventing infections diseases and protecting those vaccinated and those unvaccinated, via herd immunity. These characteristics make vaccines essential for protecting the local, national, and global communities.

The benefits of vaccines are not limited to public health; studies have shown the positive correlation between vaccination levels and productivity and economic growth Bloom (2011). Healthier individuals perform better at their duties in all age ranges, from children in schools to adults in the workplace.

Thanks to vaccines, several diseases have already been eliminated in many countries, saving millions of lives. For example, as shown in the Table 1.1, smallpox, diphtheria, and polio have been virtually eradicated in the U.S. and other western countries. However, the situation is different for low-income and low-middle-income countries (LIC and LMIC). The WHO, UNICEF and GAVI estimates that, annually, 1.5 million deaths are still caused by vaccines preventable diseases, and 19.4 million children miss out on vaccination yearly UNICEF and GAVI (2020).

Aside from lack of financial support, the main bottleneck that affects vaccination rates in LIC and LMIC, is the supply chain, as exposed by Kaufmann, Miller, and Cheyne (2011) and Zaffran et al. (2013). On the one hand, the immunization supply chain (ISC) in many LIC and LMIC was developed in 1970 (Lee et al. (2015)), making them outdated and unsuitable for the current demands and cold chain requirements. On the other hand ISC can not handle the increasing volume



Disease	20th Century annual morbidity	2016 Reported cases	Percent decrease (%)
Smallpox	29,005	0	100
Diphtheria	21,053	0	100
Measles	530,217	69	>99
Mumps	162,344	5,311	97
Pertussis	200,752	15,737	92
Polio (paralytic)	16,316	0	100
Rubella	47,745	5	>99
Congenital rubella syndrome	152	1	99
Tetanus	580	33	94
Haemophilus influenzae	20,000	22*	>99

**Haemophilus influenzae* type b (Hib) < 5 y of age.

Figure 1.1: Comparison of annual morbidity in 20th Century and current cases of vaccine-preventable diseases in the U.S. (Orensteina and Ahmedb (2017)).

of vaccines. For example, the number of antigens that the WHO recommends for vaccination programs has doubled from 6 to 12 in the last decades, and the volume of the population in vaccination programs has increased drastically, due to the increment of population (Figure 1.2).

Lately, the international segment of the ISC has been specially stress due to Covid Pandemic, the Ukraine-Russia conflict and its consequences. These disruptions have translated in drastic reductions in shipping capacity (Anurag Kotoky (2020)), up to tenfold increments in freight rates (*Is there an end in sight to supply chain disruption? | Financial Times* (n.d.)), shortages, and oversupply of Covdi-19 vaccines leading to resources wastage (Edward Mcallister (2021)).

Due to the relevance of current events, this investigation will focus on handling the effect of supply disruptions on the global vaccine procurement system managed by UNICEF for LIC and LMIC. This investigation is funded on the idea that disruptions in the distribution capacity at the international level could be mitigate optimally from the operations research (OR) point of view. The hypothesis is that countries could be rank according to some priority levels and the shipments could be re-route. The goal is to find an answer to the research question (RQ): How to optimally prioritize the delivery of procurement orders for multiple vaccines when distribution capacity is interrupted.

The vaccine market in many LIC and LMIC countries is organized by pool procurement schemes. LIC and LMIC share their demand projections and vaccination routines with procurement agents such as UNICEF or PAHO. These agents

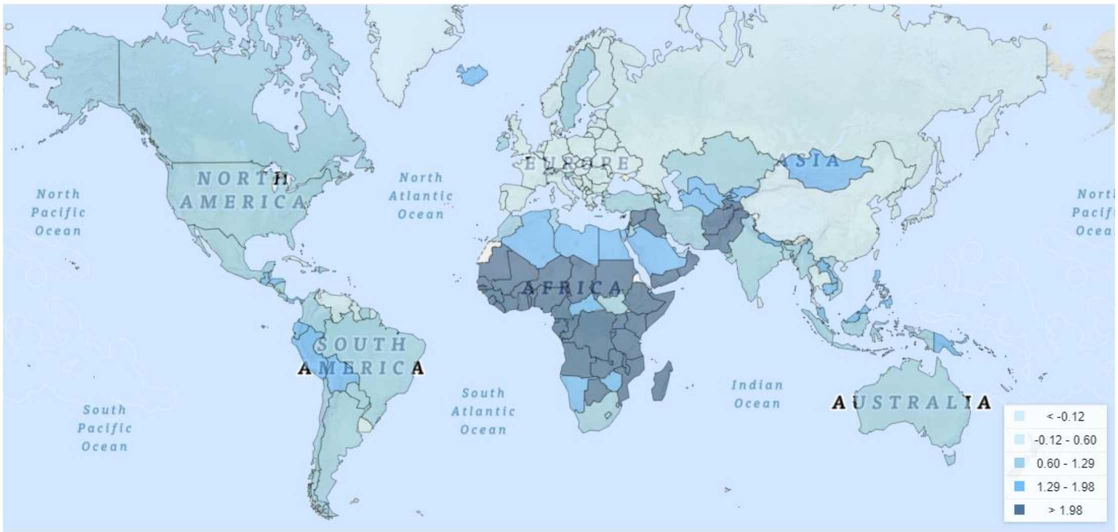


Figure 1.2: Population growth (annual %) (World Bank (2019)).

aggregate the countries' orders into a single tender for suppliers. The advantages of this market structure is the price reduction thanks to economies of scale and tiered pricing. From the supplier perspective, pool procurement hedges payment and demand uncertainty and increases their market reach (Helen Saxenian, Arias, Bloom, Cashin, and Wilson (2017)). Aside from designing vaccine tenders and managing the procurement of the vaccine orders, UNICEF also assists LIC countries in developing annual demand projections and handling the distribution of vaccine orders by antigen according to the country's immunization schedule. This research is focus on the last point, in finding an answer for the RQ from the point of view of the distribution of procurement orders (PO)[1] managed by UNICEF.

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[1] Vaccine orders are referred as procurement orders.

Chapter 2

Literature Review

This section presents the literature on which this study is based. Firstly the factors that determine the spread of disease and the usability of vaccines were studied. Lastly, the literature review focuses on handling transportation disruption from the OR perspective.

2.1 Usability of vaccines & spread of diseases

To decide the criteria that affect the utilization of vaccines, the literature available on disease spread, vaccine coverage, and vaccine supply chains was explored. Regarding vaccine coverage, David E. Phillips et al. (2017) was among the most influencing papers for this investigation. The paper describes three main clusters of factors afecting vaccine coverage. Firstly, the intend to vaccinate. It include the view of vaccination in the society, how accepted vaccination is and the trustness of the population in vaccines. Secondly, the facilities readiness. It includes all the factors related with the logistics of vaccinations, including the state of the supply chain as well as the availability of educated personal. The last cluster include how accessible vaccinations points are to the population, which is affected by the density of the areas as well as the number of health centers.

Regarding disease spread, Kate E Jones et al. (2008) studied infectious outbreaks between 1940 and 2004. They conclude that zoonotic emerging infectious diseases were highly related to the human population density and its growth, the rainfall as well as the latitude of the country. The book Institute of Medicine (US) Committee on Emerging Microbial Threats to Health in the 21st Century (2003) makes a much deeper study of the factors related to emerging infectious diseases in chapter 3. The authors cluster the factors in different categories. Those most relevant to the research are going to be developed.

The first category mentioned is the human susceptibility to infection. Inside

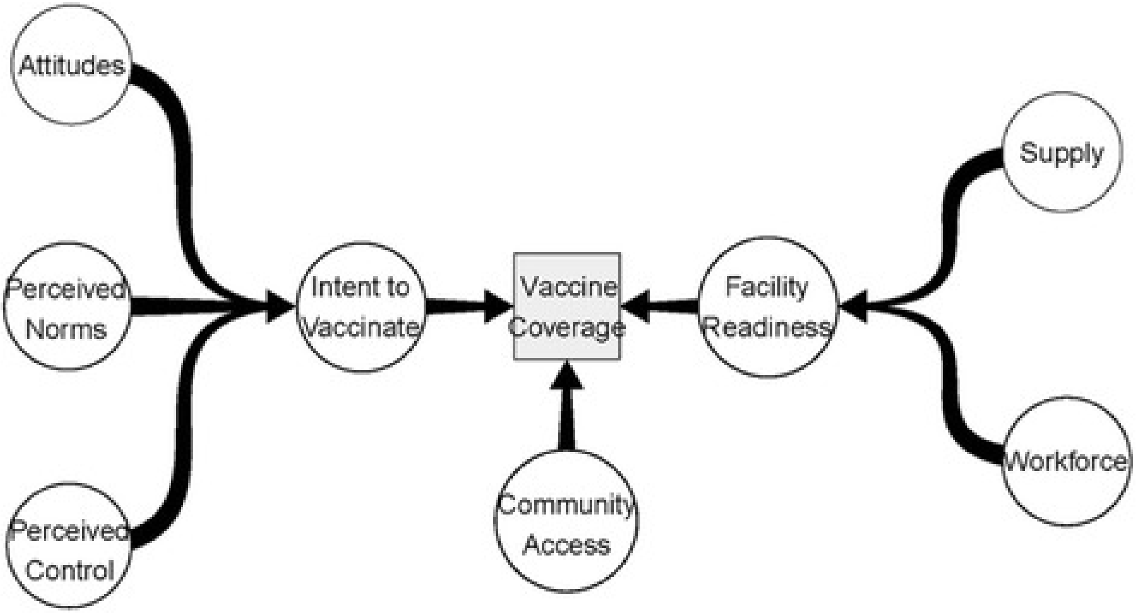

Figure 2.1: Conceptual framework for vaccine coverage (David E. Phillips et al. (2017)):

this category, the author discusses how biological factors affect our susceptibility to certain diseases. Most of the criteria under this category are not easy to quantify and, therefore, are not suitable for the ranking of PO, except for Malnutrition. The second category is climate, where the author derived the same conclusion as Kate E Jones et al. (2008). Both considering rainfall a critical factor for spreading diseases. The third category cluster human demographics and human behavior. The indicators include population growth, urbanization, and the aging of the population. Older people tend to be more likely to be affected by diseases.

Lastly, the fourth category includes international travel and commerce. The movement of people and goods acts as transmission vectors that can rapidly increase the transmission rate of diseases. In addition, others categories such as war and famine, and political will were describe as factors affecting the spread of diseases.

World Health Organization (2009) study the effectiveness of the vaccination programs. They point out that low vaccination rates and missing the vaccination targets in multiple Sub-Saharan countries is related primarily to the lack of financial investment in the health system and vaccination programs, as well as the density of health workers. Secondary factors include government in-stability and corruption were also consider.

2.2 Disruption handling at the ISC

The literature about the vaccines logistic from the OR field is clustered in decision-problems around four main areas, product design, production optimization, vaccine allocation, and distribution. The first two areas focus on designing and determining what vaccines to produce, how many, and when. The third area focuses on deciding which groups to vaccinate. Lastly, the distribution cluster, the most relevant to our investigation, focuses on the routing and scheduling of orders, and inventory control (Duijzer, van Jaarsveld, and Dekker (2018)).

Sazvar, Tafakkori, Oladzad, and Nayeri (2021) proposes a study based on a similar approach to the proposed investigation. He focuses on determining the supply chain at a national level, optimizing for handling disruptions while mitigating environmental concerns. In order to cope with the uncertainties affecting the supply chain, the authors rely on a robust fuzzy optimization approach and a multi-objective model for optimizing various objectives such as minimizing cost, total pollution, and deviations from ideal social responsibility.

De Boeck, Decouttere, Jónasson, and Vandaele (2021) also focuses on the national level vaccine supply chains and uses simulation and spatial modeling to suggest how to prevent the stock-out in areas prone to meteorological disruptions.

Regarding the problem of handling disruptions, the research was focused on the airline industries disruptions, given that air transportation is the primary mode of distribution for international vaccine shipments. Jens Clausen, Larsen, and Rezanova (2010) reviews the current state-of-affairs for managing disruptions in the airline industry. In order to re-schedule the flights, the author classifies approaches according to the solution method. It includes solutions based on network flow algorithms, and time-band networks, as the most suitable methods.

Chapter 3

Methodology

3.1 Approach

In order to answer the RQ, A two-stage decision model is proposed. The first stage ranks each PO considering multiple criteria. The second stage determines the optimal allocation plan of the POs. It considers, as inputs, a ranked set of PO and the available distribution capacity. The full implementation of the model could be observed in Figure 3.1.

The model is based on the assumption that future demand capacity is not predictable and therefore only the current available transportation is known. This occurred in highly uncertain situations, such as the first six months of the Covid-19 pandemic, the Ukraine-Russian war of 2022, and other events where it was impossible to forecast the available distribution capacity.

3.2 Procurement order prioritization model:

To rank a list of past due and upcoming PO under insufficient capacity, we propose a model that considers multiple criteria from different drivers of vaccines utilization. The output of this model is going to be used as a proxy for the "Value" of each PO. The concept of "Value" is one of the main contribution of this research. It can be understand as the reward for full filling one vaccine dose of a given PO. The model is based on Analytical Hierarchy Process (AHP).

3.2.1 AHP

Thomas L. Saaty developed AHP in 1970 to facilitate complex decision-making. This method allows decision-makers to rank alternatives, in this case PO, by mak-

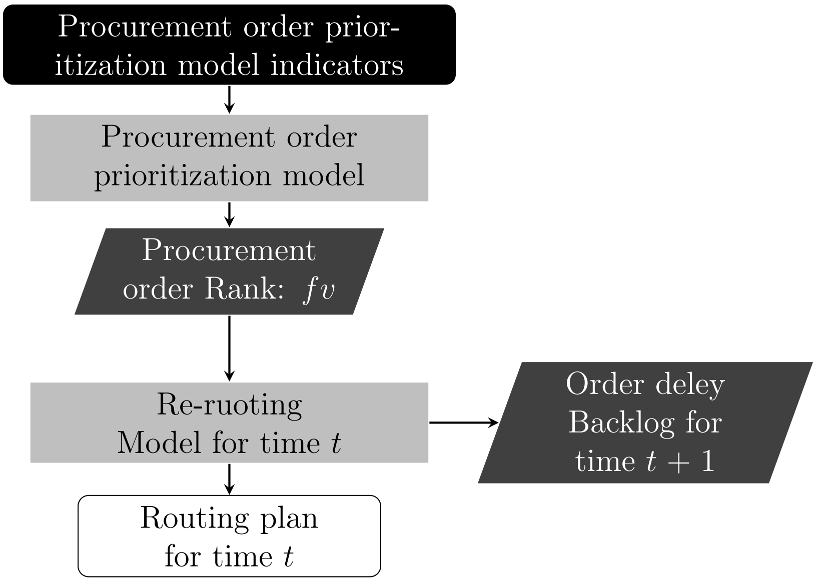

Figure 3.1: Full model flowchart.

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ing a simple pairwise comparisons. This method was selected because three main reasons:

- Easy to understand: The simplicity of pairwise comparisons makes the models based on AHP easy to understand, even for those unfamiliar with the development of the model. This is key as complex mathematical models are often perceived as a black box, making decision-makers distrust them due to their opacity.
- Easy to implement: AHP can be easily expanded. Criterias and subcriterias could be added or remove according to decisions makers expertise.
- Extensive research: AHP has been the focus on many studies and is widely used in areas such as health care, resources allocation etc.

The computation of AHP is further explained in Appendix C .

3.2.2 Criterias and subcriterias:

After a literature review about the drivers of vaccine coverage, the transmission of diseases, and the supply chain of vaccines for LIC and MLIC, a set of criteria and subcriteria were selected. They are shown in Figure 3.2.

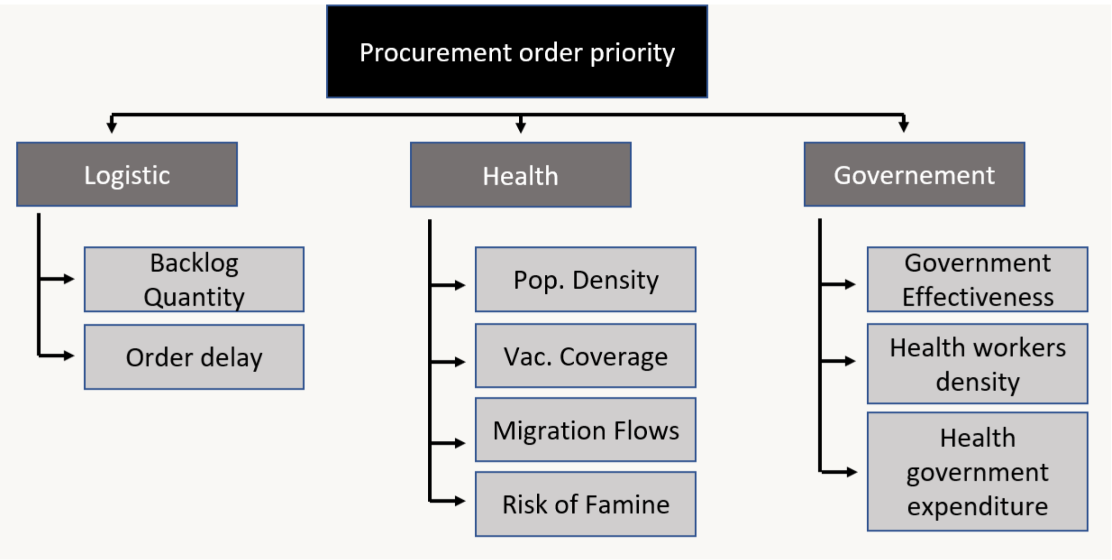


Figure 3.2: AHP criterias and subcriterias for PO ranking in LIC and MLIC.

Logistic aspect: These criteria include all the elements of the country's supply chain characteristics that could affect the usage of the vaccines.

- Order delay: Delays in PO are especially important for two reasons. Firstly, the vaccine's short shelf life and secondly, delays could lead to stock-outs, that could halt immunization programs.
- Backlog: The size of the backlog demand for each PO.

Additional sub-criteria such as the cold chain capacity should also be considered. Vaccines needs to be maintain within specific temperature ranges and therefore it is a critical factor in the logistic of vaccines. Due to the lack of data, this subcriterias was not introduced in the model.

Health aspect: The second criteria groups the factors related to the spread of diseases and the necessity of vaccines from the health point of view.

- Population density: Diseases breakouts in highly populated areas have high transmissions rates than rural areas or cities with low population density.
- Vaccine Coverage: PO that have as destination countries with low vaccines coverage's should be prioritize.

- Migrations flows: As described in the literature review, the movement of the population acts as a transmission vector, making countries or cities with high flows of population and commerce prone to the spread of diseases
- Risk of Famine: Famine is linked to a weak immune system, which makes those with famine more likely to get infected and respond worse than those with proper nutrition.

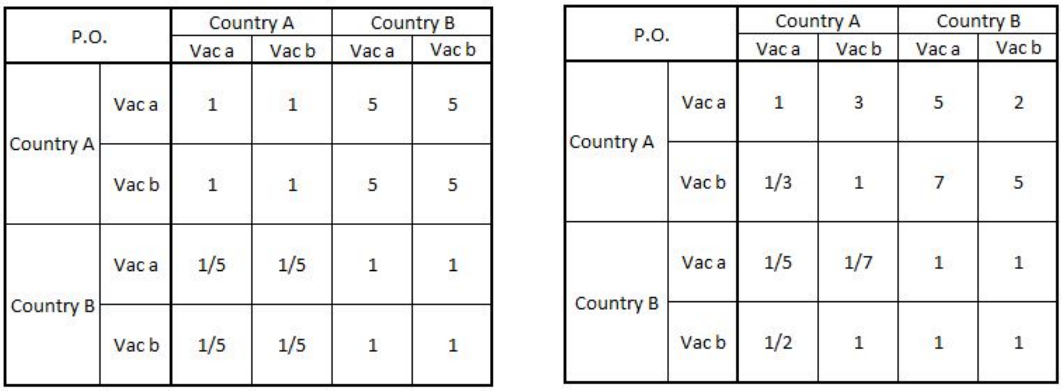
Government aspect: The last criteria includes the factors that relates the country political and government structure with vaccination ussage.

- Government stability: This criterion is in charge of comparing countries in terms of stability. In order to measure how stable or reliable a country is in political terms, the Worldwide Government indicators will be used. This indicators computes six indicators thanks to historical data from the World Bank and other institutions. These indicators include Control of Corruption, Government Effectiveness, or Political stability. Kraay, Kaufmann, and Mastruzzi (2010) Government stability is an example of challenging sub-criteria as country stability is critical to vaccine usage efficiency, but political instability is highly correlated with outbreaks of Polio or DPT, making vaccines more needed Venkatesan (2022) Arsenault et al. (2017)
- % of GDP invested in Health: A robust public health system is necessary for correctly distributing and handling vaccines. In order to measure the robustness of the public health system the % of GDP invested in health is used as a proxy.
- Health workers density: One issue of vaccine usage is the lack of qualified workers. They are essential to the correct administration of the vaccines as well as to reduce the waste of vaccines. This factor is especially critical as qualified health workers usually migrate to more developed countries to improve their living standards.

3.2.3 Evaluation of Criteria & alternatives:

In traditional AHP implementation, the pairwise criteria is done by experts that evaluate all the alternatives. In this case, the alternatives are going to represent each PO. The number of pairwise comparations is considerably large due to the large number of alternatives (Number of Countries $*$ number of vaccines). To solve that issue the pairwise evaluation of the alternatives PM_{ij} is computed automatically by measuring the difference between the proxies I_i associated with the different sub-criteria (Eq C.1). Each sub criteria is associated with a country or a vaccine in a hierarchical way. If an indicator is associated with the country level, all the alternatives under the country level will have the same pairwise comparison. An example can be observed at Figure 3.3b.

$$PM_{i,j} = I_i^{sc} - I_j^{sc} \quad \forall \quad i,j \in \text{Pairwise matrix} \quad \forall \quad sc \in \text{Subcriterias} \tag{3.1}$$



P.O.		Country A		Country B	
		Vac a	Vac b	Vac a	Vac b
Country A	Vac a	1	1	5	5
	Vac b	1	1	5	5
Country B	Vac a	1/5	1/5	1	1
	Vac b	1/5	1/5	1	1

(a) Country based criteria.

P.O.		Country A		Country B	
		Vac a	Vac b	Vac a	Vac b
Country A	Vac a	1	3	5	2
	Vac b	1/3	1	7	5
Country B	Vac a	1/5	1/7	1	1
	Vac b	1/2	1	1	1

(b) PO based criteria.

Figure 3.3: Pairwise matrix (PM) example.

Decision makers intervention

The main difficulty of this approach is the dichotomy of the comparations. Countries, where vaccines are needed the most tend to have lower efficiency in vaccine usage. This approach tries to balance this dichotomy with the weights selection. Decision-makers will be able to adjust the weight of the different criterias to take into account this dichotomy.

The advantage of this model is that the numbers of decisions needed is considerable low and easily manageable. With this approach decisions makers are able to focus its resources and to reduce possible conflict of interest.

3.3 Re-routing model:

The second stage is based on a linear programming model. The ISC is modeled based on an network flow represetation. The main idea behind network flow models is the use of nodes and arcs. Nodes will represent the location of producers and consumer and links will represent the available distribution capacity between nodes. With the help of commercial solvers and optimal solution for the system is found. This solution will minimize a cost function (CF) (Eq 3.2). The solution will represent the vaccines of each PO that should be shipped in a given flight.

The model has two key characteristics. Firstly the CF includes the monetary cost associated with the cost of vaccines and the distribution cost as well as the concept of "Value". It was computed from the first stage of the proposed solution. With this approach the optimal solution will minimise the cost while maximizing the "Value".

Secondly this model is able to use nodes as hubs. Vaccines will be able to be ship to an intermediate node. This increases drastically the possibilities of full-filing the POs, as there will be more paths available to the countries.

This model architecture was choose due to its simplicity to be solve. The main limitation of linear programming models is that although an optimal solution could be found for small test cases, is often the case where in big real world scenarios, commercial solvers are not able to find the optimal solution. Network flow models have a particular mathematical topography which make them easy to solve, even for high dimension problems.

3.3.1 Mathematical model:

Sets:

Co: Countries.

Man: Manufacturers.

No: $Co \cup Man$

Tv: Type of vaccines.

Parameters:

dc_{ijv}**:** Distribution cost ($) per vaccine leaving node i with destination the node j

$$\forall \quad i \quad \in \quad No \quad \forall \quad j \in No \quad \forall \quad v \in Tv$$

fv_{jv}**:** "Value" from fulfilling the demand of vaccine v from the country j

$$\forall \quad j \quad \in \quad Co \quad \forall \quad v \in Tv$$

vc_{jv}**:** Cost($) per unit of vaccine v from the manufacture j

$$\forall \quad j \quad \in \quad Man \quad \forall \quad v \in Tv$$

ac_{ij}: Available shipping capacity from node i to node j

$$\forall \quad i,j \in No$$

nd_{iv}: Net demand for each node i and for each vaccine type v. (negative = offer(manufacturers), positive = consumer(countries)

$$\forall \quad i \in No \quad \forall v \in \quad Tv$$

α: Configuration parameter.

β: Configuration parameter.

γ: Configuration parameter.

M_{AMD}: Control constant 1.

M_{AMS}: Control constant 2.

Decision variables:

X_{ijv}: Number of vaccines of type v leaving manufacture i with destination the country j

$$\forall \quad i,j \quad \in \quad No \quad \forall \quad v \in Tv$$

AMD_{iv}: Accumulated missing demand for each node i for the type of vaccine v

$$\forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv$$

AMS_{iv}: Accumulated missing stock for each node i for the type of vaccine v

$$\forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv$$

F_{iv}: Fulfill demand for each node i for the type of vaccine v

$$\forall \quad i \in Co \quad \forall \quad v \quad \in \quad Tv$$

Formulation:

Min:

$$\beta \sum_{i,j \in No} \sum_{v \in Tv} X_{ijv} dc_{ij} + \gamma \sum_{i \in Man} \sum_{j \in No} \sum_{v \in Tv} X_{ijv} vc_{iv} - \\ \alpha \sum_{j \in Co} \sum_{v \in Tv} F_{jv} fv_{jv} + \sum_{i \in No} \sum_{v \in Tv} (M_{AMD} AMD_{iv} + M_{AMS} AMS_{iv}) \quad (3.2)$$

s.t.

$$\sum_{v \in V} X_{ijv} \leq ac_{ij} \quad \forall \quad i,j \quad \in \quad No \quad \forall \quad v \quad \in \quad Tv \tag{3.3}$$

$$\sum_{i \in No} X_{ijv} - \sum_{i \in No} X_{jiv} = nd_{j,v} - AMD_{j,v} + AMS_{j,v} \qquad \forall \quad j \quad \in \quad No \quad \forall \quad v \quad \in \quad Tv \tag{3.4}$$

$$F_{iv} = nd_{i,v} - AMD_{iv} \quad \forall \quad i \quad \in \quad Co \quad \forall \quad v \quad \in \quad Tv \quad \forall \quad t \in T \tag{3.5}$$

$$F_{iv} \geq 0 \quad \forall \quad i \in Co \quad \forall \quad v \quad \in \quad Tv \tag{3.6}$$

$$X_{ijv} \geq 0 \quad \forall \quad i,j \quad \in \quad No \quad \forall \quad v \in Tv \tag{3.7}$$

$$AMS_{j,v}, AMD_{j,v} \geq 0 \quad \forall \quad j \quad \in \quad No \quad \forall \quad v \in Tv \tag{3.8}$$

Constrains explication:

3.2 Objective cost function: It computes the looss of the routing. It considers the Value fv as a proxy for the income. Additional configuration parameters are used to adjust the units as well as to consider or not a certain element of the cost, such as distribution cost or vaccines cost. Parameters M_{AMD} and M_{AMS} are used to penalized the slack variables

3.3: This constrains force the maximun distribution capacity of each route.

3.4: Establish the net demand with backlog and slack.

3.5: Set the quantity of demand of vaccines full-filled for each type by each country.

3.6 & 3.7: Non negativity constrains.

Assumptions

Vaccines size: All vaccines have the same sizes.

Distribution capacity: It is known.

Time: It is not considered.

3.3.2 Limitations:

The main limitation of the formulation is found in the objective function. The units for dc_{ijv} and vc_{jv} are known currencies established by the user. On the other hand, the parameter fv_{jv} is unitless. In order to normalize the units, the configuration parameters β,γ, and α should be adjusted. A possible solution for this limitation is discussed in section 5.1

Chapter 4

Case study

4.1 Problem Description

In order to test the proposed solution, a case study[1] was conducted based on the international shipment of vaccines for LIC and LMIC during the year 2020. In this study, the routing plan for 45 PO from 15 selected GAVI eligible countries and a set of 3 vaccines was modeled. Due to the lack of publicly available data, the study was based on two main assumptions.

Firstly, a given vaccine's annual demand is dispatched annually in a single PO. This assumption is based on the fact that generally, the annual demand of a country is dispatched in a single order for the typical country supplied by UNICEF. Secondly, the monthly distribution capacity and POs are grouped into individual blocks. Each block will represent an instance of the proposed model and have associated parameters such as distribution capacity and net demands.

The study consists of a Montecarlo simulation, where in each stance the PO will be assigned to a random block following the procedure in Appendix D. For each Montecarlo stance, the proposed model was executed recursively for 12 iterations. Each of them representing a month of 2020. The flowchart of the integration can be observed in Figure 4.1

In order to measure the accuracy of the proposed solution, four different models will be compared, and four key performance indicators (KPI) will be measured:

Models

Different configurations of the second stage of the proposed model (Section 3.3) were compared against a BaseLine model. The different configurations can be observed in Tables 4.1 and 4.2

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[1] The model implementation, data, and the results are available in GitHub.

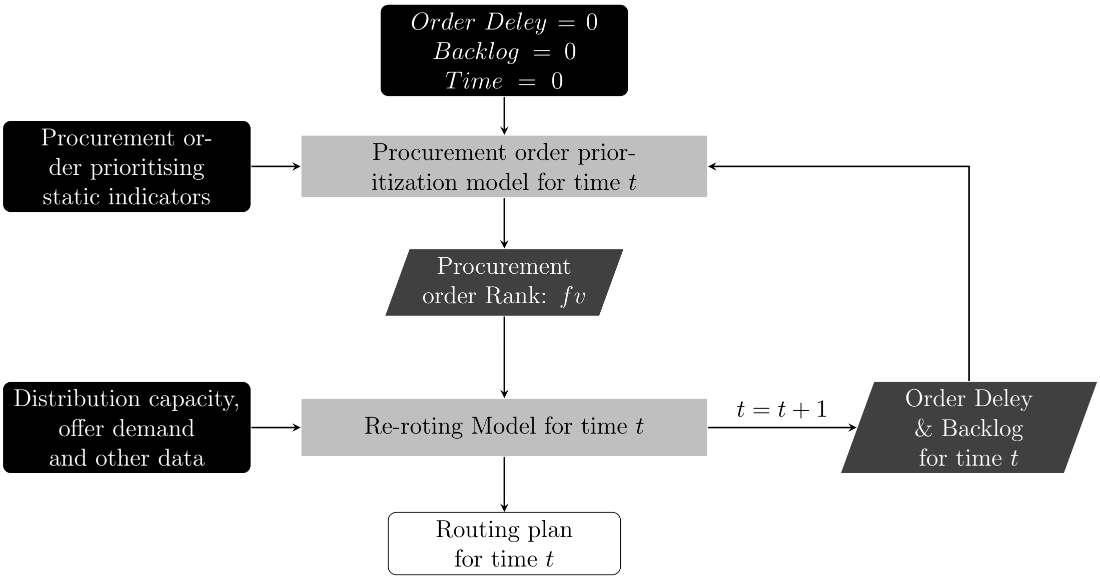


Figure 4.1: Full model flowchart.

- Baseline model (BaseLine): This model is based on a deterministic linear programming formulation. It represent the ideal situation where the annual distribution capacity is know in advance. In theory the performance of this model should be better, as it is able to plan acording to the future. It will solve the problem considering the same distribution capacity as the other models. This model will optimize for minimizing cost; it will not consider the rank from the Procurement order prioritization model to find the optimal solution. The model is described in Appendix B

- Maximization of value (MaxVal): The proposed model was set to produce a solution that maximizes the value of the vaccines.

- Minimization of cost (MinCost): The proposed model was set to produce a solution that minimizes the distribution cost.

- Maximization of value and minimization of cost: (MinMax) The proposed model was set to produce a solution that maximizes value and minimizes cost.

In table 4.2 It can be observed the configuration parameters associated to M_{AMS} and M_{AMD}. The cost associated with the demand not being fulfilled is considerably larger than the value associated with the offer. This encourages the fulfillment of the vaccine orders as the consequences of unfulfilled demand are worse than unfulfilled offer.

Regarding the parameter γ, it is set to zero in all the models to reduce similarities with the synthetic data. The data was generated minimizing distribution cost and vaccine cost. If the proposed algorithm was set to minimize the same costs, the results will be very similar.

Model	β	α	γ	Model name
Baseline	-	-	-	BaseLine
Maximization of value	0	1	0	MaxVal
Minimization of cost	1	0	0	MinCost
Minimization of cost & Maximization of value	1	1	0	MinMax

Table 4.1: Model configurations 1.

	M_{AMD}	M_{AMS}
Parameter	1000000	5000

Table 4.2: Model configurations 2.

Key performance indicators

- Total Value: This KPI represent the quality of the model. It will be calculated as the total "Value" associated to the fullfiled POs.

$$Val_t = \sum_{j \in Co} \sum_{v \in Tv} F_{jv} v_{jv} \tag{4.1}$$

$$TotalValue = \sum_{t=0..T} Val_t \tag{4.2}$$

- % of unfulfilled demand (AMD): Percentage of the demand that was not fulfilled. For models MinCost, MaxVal and MinMax, the AMD is computed as the sum of all the variables AMD of the last iteration over the total demand. For the model base, it is computed as the sum of the variable AMD for the last block.

- % of unfulfilled supply (AMS): Percentage of the stock that was not shipped. It was computed with the same approach as AMD.

- Shipping cost: The cost associated with the shipment of the vaccines

$$Cost_t = \sum_{i,j \in No} \sum_{v \in Tv} X_{ijv} dc_{jv} \tag{4.3}$$

$$TotalCost = \sum_{t=0..T} Cost_t \tag{4.4}$$

4.2 Problem Data

The main limitation of the case study is the lack of data, as much of it is not available to the public.

4.2.1 Procurement order prioritization model

The goal of this case study is to analyze the overall behavior of the full proposed solution. The analysis of how the weights of the first stage of the model (Section 3.2) affect the solution is going to be study in the future. For that reason, the weights between the different criteria and subcriteria was set to be equal. In a real-world scenario, decision-makers should adjust the weights of the different criteria and subcriteria according to the situation.

Non-logistic Indicators

The main data provider regarding country indicators were theWorld Health Organization (2022),UNICEF (2022) and World Bank (2022). They provided the following data:

- Population density per country.
- Vaccine coverage per country and vaccine.
- Movement of the population (calculated from bilateral migration data).
- Current health expenditure (% of GDP).
- Health workers density: Nursing and midwifery personnel (per 10 000 population).

Regarding the data that quantify the Risk of Famine it was sourced from the Global Hunger Index (Concern Worldwide and Welthungerhilfe (2022)). Lastly, the Government effectiveness was sourced from the Worldwide Governance Indicators project (Daniel Kaufmann (2022).

The data was selected from the latest year available, in most cases, 2020. During all the 12 iterations, the non-logistic indicators for the Procurement order prioritization model were assumed to be static. This assumption is valid as the change rate of the non-logistic indicators such as population density or health workers density can be considered zero within one year.

Logistic Indicators

The delay of the orders and the accumulated missing demand were sourced from the previous iteration, as shown in Figure 4.1. In the case of the first iteration, the delay and the accumulated missing demand were set to zero.

4.2.2 Vaccine supply

UNICEF (2022) provided the annual aggregated demand for the selected countries and vaccines during 2020. As well as the cost of the vaccine dose per manufacture.

4.2.3 Demand and Shipping capacity

Two key data sets were unavailable: the distribution capacity and cost. It was generated synthetically following these assumptions:

- Demand equal to supply: According to the World Health Organization (2009) due to the market dynamics of the vaccination market for LIC and LMIC, supply and demand agree to the orders to produce beforehand, making supply meet demand. Therefore there is no excess capacity. In this case study, it was assumed that the aggregated offer for each vaccine was equal to the aggregated demand per vaccine.

- Distribution cost is based on kg per km shipped, and it is fixed for all routes. The proxy used to calculate the shipment cost was the revenue per mille tonne of air freight companies in the U.S. in 2020 provided by Bureau of Transportation Statistics (2020).

- The route length was based on the straight line distance between the country's capital and the manufacturer's country's capital. The data was provided by Distancia.co (2022).

- The available routes were generated by a linear programming problem described in Appendix A. This problem considers vaccine price per manufacturer, the shipping cost, and the country's demand which provides a solution that minimizes the distribution cost and the vaccine cost.

- Based on the assumption that most of the shipment of vaccines is transported as cargo belly of passenger flights. The reduced distribution capacity will be based on the ratio of monthly international passengers in 2020 over 2019 (Figure 4.2). It is assumed that the reduction of cargo belly capacity will be reduced by the same ratio as passenger seats.

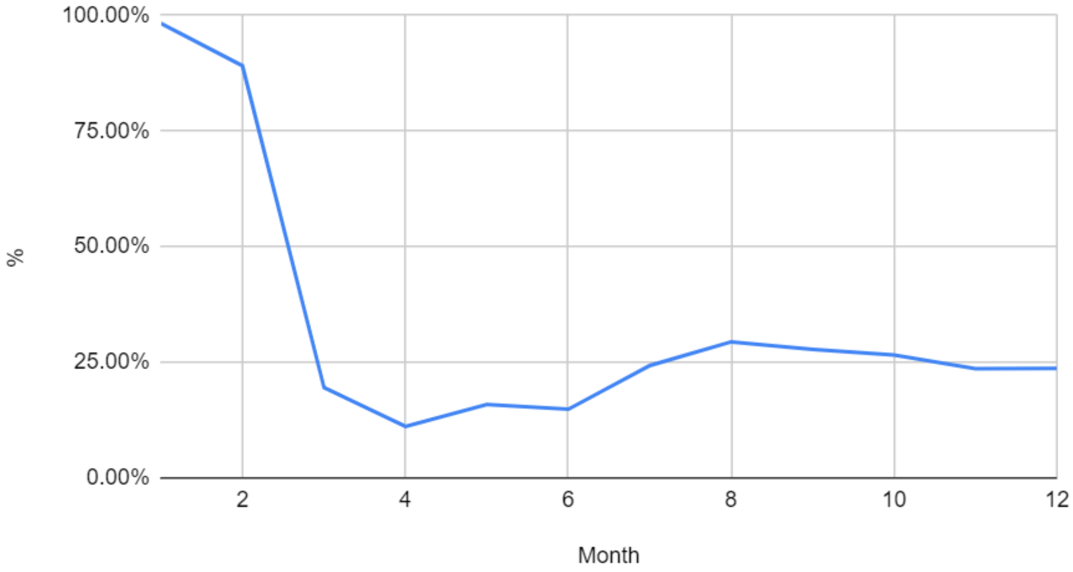


Figure 4.2: Reduction of international seats of the period 2019 vs 2020.

4.2.4 Other considerations

The distribution cost was normalized to values ranging from 0 to 10000. In the case of the fulfillment value, the output of the PO prioritization model (3.2) was scaled to the same range as the distribution cost range.

4.3 Results

4.3.1 Model verification

To verify that the model was implemented correctly and the synthetic data was generated correctly a series of tests were conducted. Firstly the models were executed without reduction of the distribution capacity. As expected the metrics AMD and AMS were zero as all the offer was sent to the demand. Secondly, a stance of the Montecarlo simulation was analysed. A limitation of the data generation algorithm was discovered. The synthetic routes are very constrained and direct. This force the model to always use the same routes. It is not able to use the nodes as hubs. This behavior can be observed in Figure 4.3, vaccines are send from the manufacture to the final destination. The routing for the 4 models were compared, the only difference was found in the amount of vaccine sent. This limitation do not invalidate the case study, but it should be consider.

For the same stance of the Montecarlo simulation the accumulated missing net

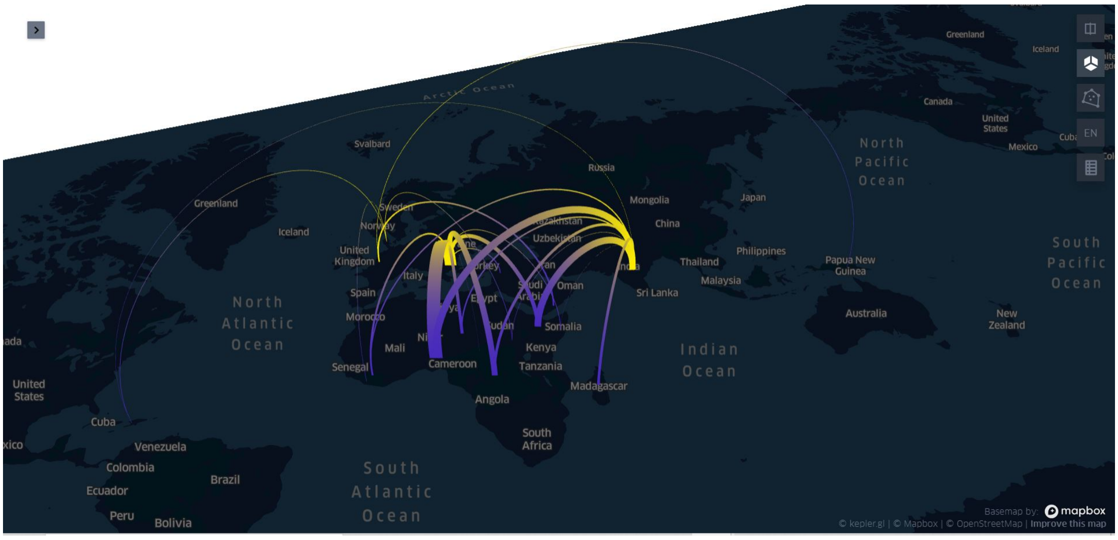
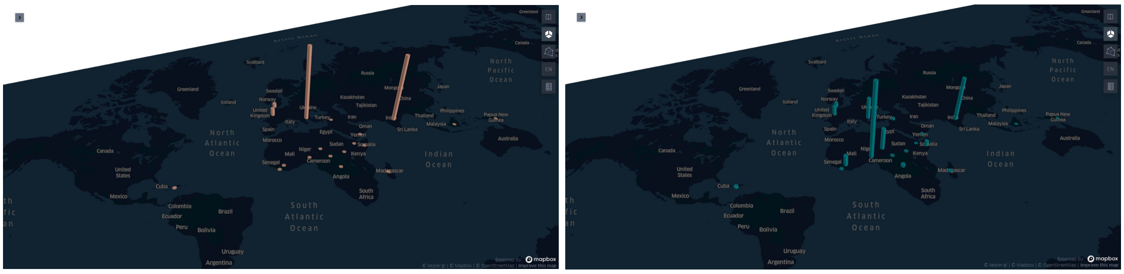


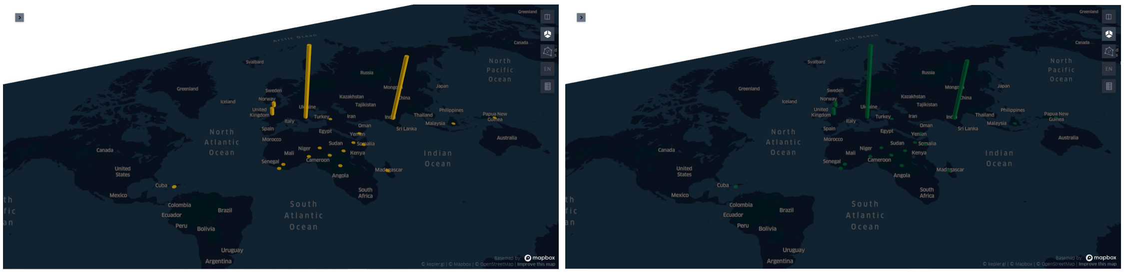
Figure 4.3: Routes: model BaseLine. (from: yellow, to: purple).

Figure 4.4: Manufactures(blue) and consumers countries (red) location.

demand, the full-filed orders and it associated value was studied as shown in the Figures 4.5, 4.6, 4.7. The mayor difference in the results is only found for the accumulated missing net demand. In Figure 4.5 all the models but MaxVal have the same pattern. In the case of the model MaxVal the missing net demand has been shifted from manufactures to the consumers countries. The reason for this output is that the parameter M_{AMD} from the second stage of the proposed model is too low, making the cost of distributing to certain countries higher than the cost of not distributing.

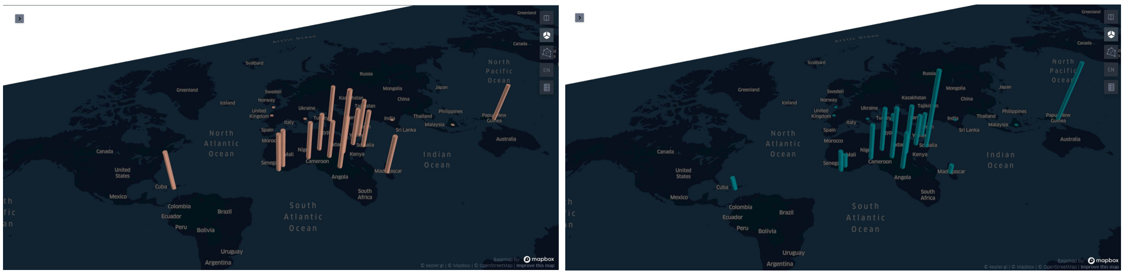


(a) Model: BaseLine. (b) Model: MaxValue.

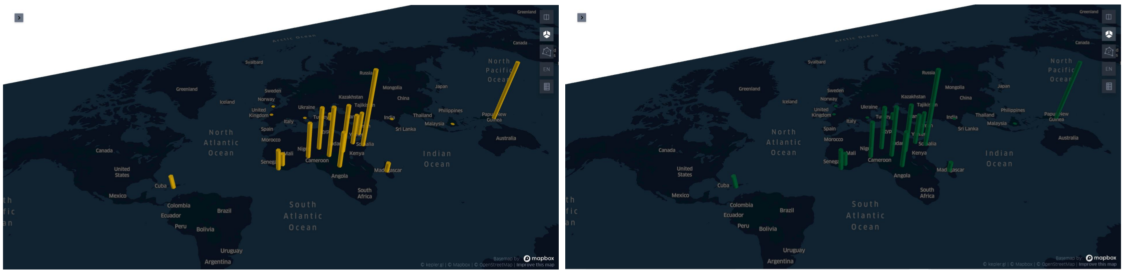


(c) Model: MinCost. (d) Model: MinMax.

Figure 4.5: Accumulated missing net demand.

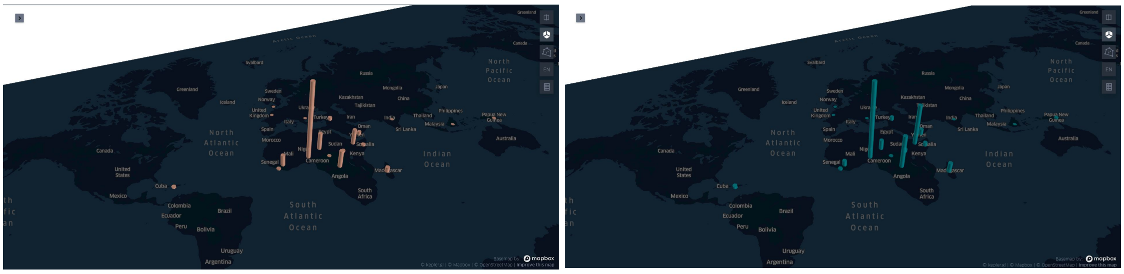


(a) Model: BaseLine. (b) Model: MaxValue.



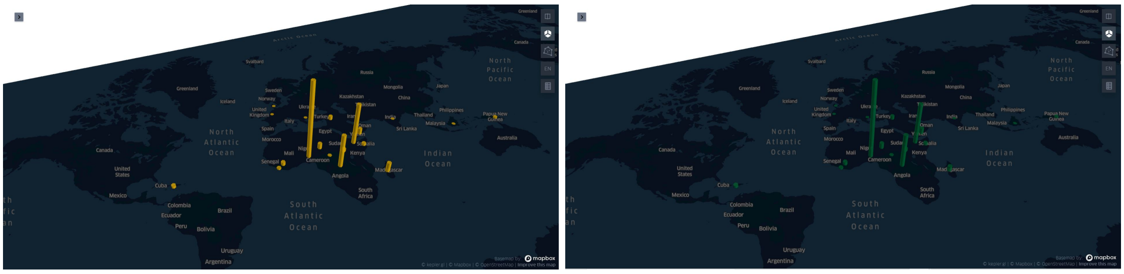
(c) Model: MinCost. (d) Model: MinMax.

Figure 4.6: "Value" of the fulfilled demand.



(a) Model: BaseLine.

(b) Model: MaxValue.



(c) Model: MinCost.

(d) Model: MinMax.

Figure 4.7: Fulfilled demand.

4.3.2 Outcome

	Value		Cost		Amd		Ams	
	Avg	Std	Avg	Std	Avg	Std	Avg	Std
MinCost	2.65E+07	7.71E+05	3.15E+10	7.37E+08	81%	2%	81%	2%
MaxValue	4.42E+07	1.04E+06	5.13E+10	1.19E+09	71%	2%	70%	2%
MinMax	2.81E+07	7.59E+05	3.15E+10	7.37E+08	81%	2%	81%	2%
BaeLine	2.90E+07	7.83E+05	3.69E+10	8.90E+08	78%	2%	78%	2%

Table 4.3: Aggregated results after outliers elimination.

Value	Cost	AMD
158%	163%	12.28%

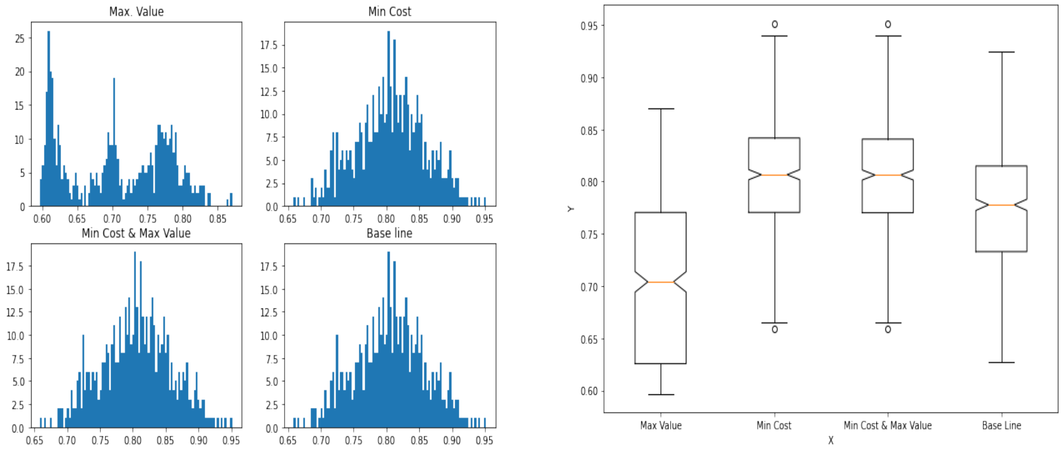
Table 4.4: MaxValue improvement over MinMax

The filtered results from the simulations can be observed in Table 4.3. Outliers were eliminated in order to reduce the standard deviation of the results. The Montecarlo stances were reduced from 600 to 501.

Firstly it can observed that the KPIs AMD and AMS associated with each model has the same value. The reason for this is the lack of excess capacity of manufacturers. If we compare the same KPI between the different models, the best performance is found in the model MaxValue. It is 10% points lower than the worst models in terms of AMD. We can observed that the distribution cost is negatively correlated with the KPI cost, and positively correlated with the KPI Value. This behavior is explain because an increment of vaccine shipment means distribution cost and more fullfiled orders.

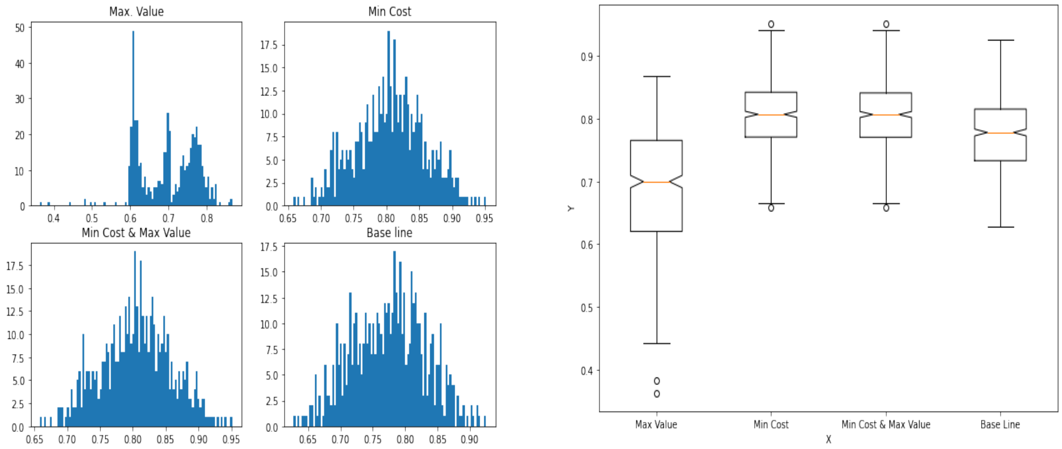
Due to the high standard deviation, the models were analyses quantitative and qualitative. Firstly, the Whisker and box plots and the histograms were studied. The models BaseLine and MaxValue present clearly different distribution. In the other hand the models Min Cost and MinMax were really similar. After a Kolmogorov Smirnov Test, it could not be confirmed that the models share different distributions. The reason for the similarity of this two models is imputed to a biased of the CF toward minimizing the distribution cost. In a model without bias, the model MinMax should yield results between the model MinCost and MaxValue, as Cost and Value are negatively correlated. The reason for this biased is the unit conversion between the units used for the "Cost" and the "Value".

Over all the best performing model in terms of AMD and Value is MaxValue. The improvements of the model over MinMax are presented in Table 4.4. The improvement of Value and cost are similar, while the metric AMD is reduced a 12%.



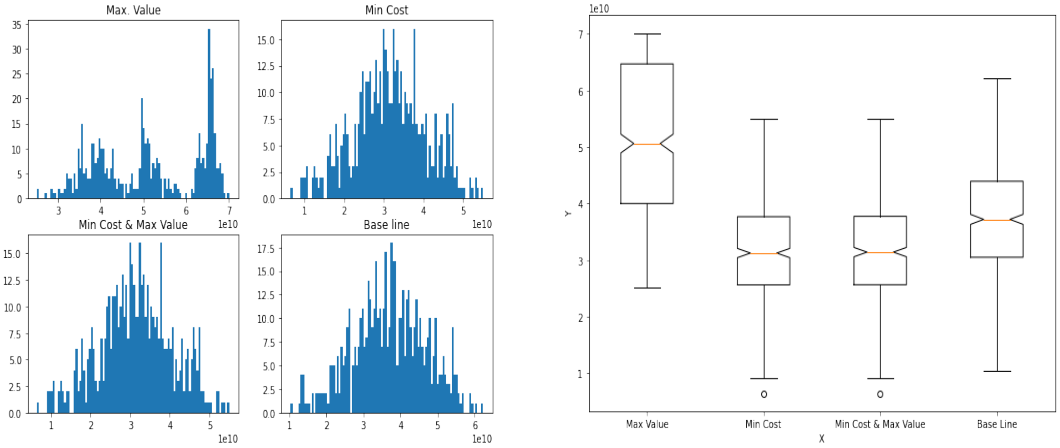
(a) Histogram (b) Whisker and box

Figure 4.8: KPI: AMD



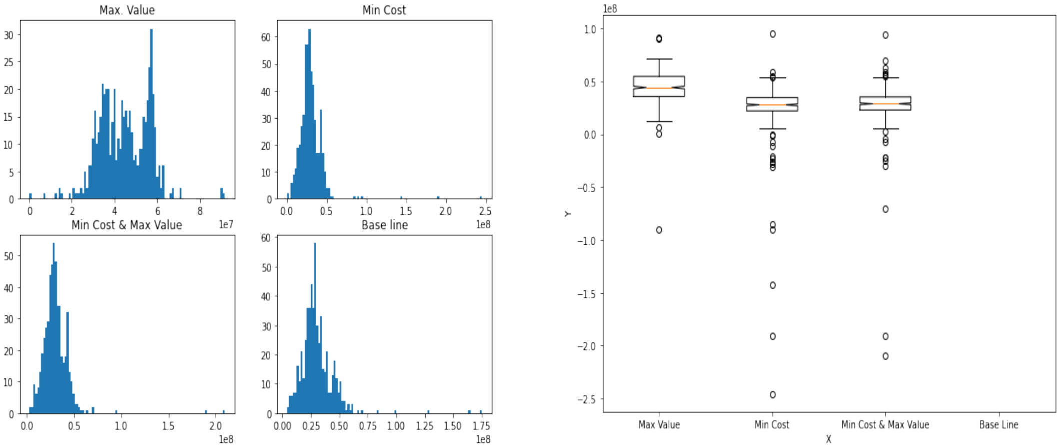
(a) Histogram (b) Whisker and box

Figure 4.9: KPI: AMS



(a) Histogram (b) Whisker and box

Figure 4.10: KPI: cost



(a) Histogram (b) Whisker and box

Figure 4.11: KPI: Value

Chapter 5

Discussion & Conclutions

5.1 Futer work and discussion:

The main limitation of this investigation was the lack of real data regarding the distribution capacity. The synthetic data used in the case study helped validate the overall behavior of the proposed model, but it did not allow us to exploit its possibilities fully. The next step of this research is to complete the validation of the model by the study of the model with a data set that includes connections between countries and manufacturers. These connections will allow us to test the feature of using nodes as hubs.

In addition, new Montecarlo experiments could be simulated, where the distribution capacity is reduced to random routes instead of reducing it globally by a given percentage. This scenario would be closer to reality; in a real-world scenario, the cancellation of routes is more common than reducing capacity.

The case study highlighted two limitations of the model. High distribution costs and the possibility of bias in the model. Currently, a solution to solve these two limitations is being explored. The proposed model was set to just maximize "Value" ($\beta = 0$ & $\gamma = 0$). An additional budget constraint (Eq: 5.1) was added to the second stage of the proposed model. With this approach, the model is able to maximize the"value" without the possibility of bias or exceeding a given budget.

$$\sum_{i,j \in No} \sum_{v \in Tv} X_{ijv} dc_{ij} + \sum_{i \in Man} \sum_{j \in No} \sum_{v \in Tv} X_{ijv} vc_{iv} - \leq TotalBudget \tag{5.1}$$

The case study also allow us to realize that the slack variables (AMD_{ijv} and AMS_{ijv}) could be replaced by a slack variable in the maximum distribution capacity constraint (eq:3.3). This slack variable will represent the location where additional distribution capacity should be placed. Although UNICEF by default do not consider the possibility of chartering private planes, by the analysis of this slack variable decisions makers could decide if it make sense to charter the private plane, its capacity, and the route that it should follow.

5.2 Conclution

This investigation aims to answer the RQ: How to optimally prioritize the delivery of procurement orders for multiple vaccines when the distribution capacity is interrupted. The research outcome is a two-stage decision-making model to determine the optimal routing for a heavy-constrained vaccine distribution network. The first stage considers different aspects of the country's ISC state, the government reliability, and the country's health system to assign each PO a given "Value". The second stage decides the routing of the POs based on the available capacity and its value from the previous stage. The proposed model was tested successfully in a case study. Different variations of the proposed model were compared between each other and a baseline. On average, the proposed model configured to maximize "Value" had an improvement of 11% points in coverage of demand and better quality[1] but at the expense of higher cost. Several limitations of the model were found, but currently, solutions are being explored.

Although the proposed model is in an early development stage, it could be a seed to improve vaccines usability under constraint distribution capacity. The main contribution of the research is the proposed 2 stage framework and the concept of "Value". Applications of this framework are beyond vaccine distribution. It could be applied to any situation where decision-makers do not have enough distribution capacity to fulfill the demand of all the clients, and the prioritization of the orders considers multiple and complex criteria.

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[1] The quality of the model is based on the criteria "Value"

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Appendix A

Distribution capacity data generatior

The algorithm that generates the available distribution capacity and stock at each manufacturer is based on a linear programming optimization model. The model will take as input the demand of each country, the price per vaccine per manufacturer, and the distribution cost. The output will be a solution that minimizes the total cost of the operation. The data set used and the code implementation is publicly available in the repository of this research. [1]

Sets:

Co: Countries.

Man: Manufacturers.

Tv: Type of vaccines.

Parameters:

dc_{ijv}**:** Distribution cost ($) per vaccine leaving manufacture i with destination the country j at time t

$$\forall \quad i \quad \in \quad No \quad \forall \quad j \in No \quad \forall \quad t \in T \quad \forall \quad v \in Tv$$

$o_{jv} =$

$$\begin{cases} 0 & if \quad \text{vaccine v} \in \text{Tv is not provided by manufacture j} \in \text{Man} \\ M_1 & if \quad \text{vaccine v} \in \text{Tv is provided by manufacture j} \in \text{Man} \end{cases}$$

---

[1] The model implementation, data, and the results are available in GitHub.

d_{iv}**:** Demand for each country i and for each vaccine type v.

$$\forall \quad i \in No \quad \forall v \in \quad Tv$$

vc_{iv}**:** Vaccine cost for each vaccine type v and for each manufacture i.

$$\forall \quad i \in No \quad \forall v \in \quad Tv$$

M_1**:** Large constant 1.

Decision variables:

X_{ijv}**:** Number of vaccines of type v leaving manufacture j with destination the country i

$$\forall \quad i \quad \in \quad Co \quad \forall \quad j \in Man \quad \forall \quad v \in Tv$$

Formulation:

Min:

$$\sum_{i \in Co} \sum_{j \in Man} \sum_{v \in Vac} X_{ijv} \big(vc_{iv} + dc_{ijv} \big) \tag{A.1}$$

s.t.

$$X^t_{ijv} \leq ac^t_{ij} \quad \forall \quad i,j \quad \in \quad No \quad \forall \quad t \quad \in \quad T \quad \forall \quad v \quad \in \quad Tv \tag{A.2}$$

$$\sum_{i \in Co} X_{ijv} \leq o_{jv} \quad \forall \quad j \quad \in \quad Man \quad \forall \quad v \quad \in \quad Tv \tag{A.3}$$

$$\sum_{j \in Man} X_{ijv} \leq d_{iv} \quad \forall \quad i \quad \in \quad Co \quad \forall \quad v \quad \in \quad Tv \tag{A.4}$$

Appendix B

Base line model

The base line model represent the ideal model used for routing the annual demand for multiple PO. This model is consider ideal, because it considers that the future distribution capacity is known, and therefore its solution is more optimal than if only the current distribution capacity is known. The notation used follows the same structure as the second stage as the proposed model.

B.0.1 Mathematical model:

Sets:

Co: Countries.

Man: Manufacturers.

No: Co ∪ Man

Tv: Type of vaccines.

T: 0..tmax.

Parameters:

dc^t_{ijv}**:** Distribution cost (\$) per vaccine leaving manufacture i with destination the country j at time t

$$\forall \quad i \quad \in \quad No \quad \forall \quad j \in No \quad \forall \quad t \in T \quad \forall \quad v \in Tv$$

ac^t_{ij}**:** Available shipping capacity from node i to node j

$$\forall \quad i, j \in No \quad \forall \quad t \in T$$

nd_{iv}^{t}**:** Net demand for each node i and for each vaccine type v at time t. (negative = offer(manufacturers), positive = consumer(countries)

$$\forall \quad t \in T \quad \forall \quad i \in No \quad \forall v \in \quad Tv$$

M_{AMD}**:** Large constant 1.

M_{AMS}**:** Large constant 2.

Decision variables:

X_{ijv}^{t}**:** Number of vaccines of type v leaving manufacture i with destination the country j at time t

$$\forall \quad i,j \quad \in \quad No \quad \forall \quad t \in T \quad \forall \quad v \in Tv$$

AMD_{iv}^{t}**:** Accumulated missing demand for each node i at time t for the type of vaccine v

$$\forall \quad t \in T \quad \forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv$$

AMS_{iv}^{t}**:** Stock of vaccines accumulated at each node i at time t for the type of vaccine v

$$\forall \quad t_1 \in T \quad \forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv$$

F_{iv}^{t}**:** Fulfill demand for each node i at time t for the type of vaccine v

$$\forall \quad t \in T \quad \forall \quad i \in Co \quad \forall \quad v \quad \in \quad Tv$$

D_{iv}^{t}**:** Net demand + backlogging for each node i at time t for the type of vaccine v

$$\forall \quad t \in T \quad \forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv$$

Formulation:

Min:

$$\sum_{i,j \in No} \sum_{t_1 \in T} \sum_{v \in Tv} X_{ijv}^{t} dc_{jv} + \\ + \sum_{i \in No} \sum_{v \in Tv} \sum_{t \in T} \Big(M_{AMD} AMD_{iv}^{t} + M_{AMS} AMS_{iv}^{t} \Big) \quad \text{(B.1)}$$

s.t.

$$\sum_{v \in V} X_{ijv}^{t} \leq ac_{ij}^{t} \quad \forall \quad i,j \quad \in \quad No \quad \forall \quad t \quad \in \quad T \quad \forall \quad v \quad \in \quad Tv \tag{B.2}$$

$$\sum_{i \in No} \sum_{t \in T} X_{ijv}^{t} - \sum_{i \in No} \sum_{t \in T} X_{jiv}^{t} = D_{j,v}^{t} - AMD_{j,v}^{t} + AMS_{j,v}^{t}$$
$$\forall \quad j \quad \in \quad No \quad \forall \quad v \quad \in \quad Tv \quad \forall \quad t \quad \in \quad T \tag{B.3}$$

$$F_{iv}^{t} = D_{i,v}^{t} - AMD_{iv}^{t} \quad \forall \quad i \quad \in \quad Co \quad \forall \quad v \quad \in \quad Tv \quad \forall \quad t \in T \tag{B.4}$$

$$D_{i,v}^{t} = AMD_{iv}^{t-1} - AMS_{iv}^{t-1} + nd_{iv}^{t}$$
$$\forall \quad i \quad \in \quad No \quad \forall \quad v \quad \in \quad Tv \quad \forall \quad t \in Tdiff(0) \tag{B.5}$$

$$D_{i,v}^{0} = nd_{iv}^{0} \quad \forall \quad i \quad \in \quad No \quad \forall \quad v \quad \in \quad Tv \tag{B.6}$$

$$AMD_{iv}^{t_1}, \quad AMD_{iv}^{t_1}, \quad F_{iv}^{t_1} \geq 0 \quad \forall \quad t \in T \quad \forall \quad i \in No \quad \forall \quad v \quad \in \quad Tv \tag{B.7}$$

$$F_{iv}^{t_1} \geq 0 \quad \forall \quad t \in T \quad \forall \quad i \in Co \quad \forall \quad v \quad \in \quad Tv \tag{B.8}$$

$$X_{ijv}^{t} \geq 0 \quad \forall \quad i,j \quad \in \quad No \quad \forall \quad t \in T \quad \forall \quad v \in Tv \tag{B.9}$$

Appendix C

AHP algotithm

In this appendix the integration of the AHP in the first stage of the proposed algorithm is explained.

C.1 Comparation Matrix & Weight Computation

The core of AHP is the computation of the weight of the subcriteria and criteria from the comparison matrix.

PM_{nn}: N^2 Pairwise matrix comparation.

I_j^{sc}: Indicator linked to subcriteria sc and PO j.

S_j: Column j of matrix PM_{nn}

Y_{nn} : Auxiliary N^2 Matrix

F_n: Result vector

$$PM_{i,j} \;=\; I_i^{sc} - I_j^{sc} \quad \forall \quad i,j \;\in\; \text{Pairwise matrix} \quad \forall \quad sc \;\in\; \text{Subcriterias} \tag{C.1}$$

$$S_m = \sum_{n=0:N} PM_{mn} \tag{C.2}$$

$$Y_{ij} = \frac{PM_{ij}}{S_j} \tag{C.3}$$

$$F_i = \frac{\sum_{m=0:N} Y_{mi}}{N} \tag{C.4}$$

C.2 Implemantation

C.2.1 Alogrithm

The complete code is not presented as it consists of many repetitions. The code workflow follows the Algorithm 1.

Algorithm 1 AHP implementation pseudocode

```
Computation of the Pairwise comparation matrices

$MatrixDic$[main] = $AHPweight$( Main Pairwise matrix comparation )

for c $\in$ criteria do
    $MatrixDic[c]$ = $AHPweight$( Pairwise comparation matrix associated to criteria c )

    for sc $\in$ subcriterias under cirteria c do
        $MatrixDic$[c][sc] = $AHPweight$( Pairwisecomparation matrix associated to subcriteria sc )

    end for
end for

Value = Rank($MatrixDic$)
```

C.2.2 Auxiliary functions

```python
#import numpy as np
#import pandas as pd
def AHPweight(df):

  df = df.div(df.sum(axis=0), axis=1)
  df.loc['total'] = df.sum(axis=0)

  df['Weight'] = df.mean(axis=1)
  df['Weight']['total'] = np.nan
  return(df)
```

Listing C.1: AHPweight()

```
#cri = list of criterias
#sub[i] = subcriterias under the criteria i
#vac = list of vaccines
#co = list of countries
#import numpy as np
#import pandas as pd

def Rank(MatrixDic):
    Priority = np.zeros( ( len(vac)*len(co) ,1 ) )
    alpha = 100 #Scaling factor

    for i in range( len(vac)*len(co) ):
      for j,jj in enumerate(cri):
        for k,kk in enumerate(sub[jj]):
          Priority[i] = alpha*MatrixDic['main']['Weight'][j]*
              ↪ MatrixDic[jj]['Weight'][k]*MatrixDic[jj,kk]['
              ↪ Weight'][i] + Priority[i]
    return(Priority)
```

Listing C.2: Rank()

Appendix D

Randomly monthly allocation

The algorithm listed below was used to assigned the order of each country to a random block. The POs associated with a given country are assigned to a random month.

Listing D.1: Randomly order allocation

```
co_aux = Co #List of countries
rnd_co = {}
for i in range(tmax):
        rnd_co[i] = []

for i in range(tmax):
        jj = random.randint(0, 3)

        if len(co_aux) < jj:
                rnd_co[i] = random.sample(co_aux,len(co_aux))
        else:
                rnd_co[i] = random.sample(co_aux,jj)

        co_aux = list( set(co_aux) ^ set(rnd_co[i]) )

        for c in rnd_co[i]:
                for v in Tv:
                        t_prog[c,v] = i

        if i == (tmax-1):
                rnd_co[i] = random.sample(co_aux,len(co_aux))

        for c in rnd_co[i]:
```

```
                        for v in Tv:
                                t_prog[c,v] = i

                if len(co_aux) == 0:
                        break
```

Appendix E

Sustainable Development Goals

The results of this investigation will contribute to the UN Sustainable Development Goals (SDG) (United Nations (2022)), especially SDG 3 (Good Health and Wellbeing), SDG 10 (Reduced Inequality), and SDG 17 (Partnerships to achieve the Goal).

The research proposes a system to assist decision-makers in situations where vaccine distribution capacity for LIC and LMIC is reduced drastically. The model is based on mathematical optimization, whose main criterion is to maximize vaccine usage. Therefore, more citizens could have access to those vaccines. The results from this research could act as a seed to improve the population's health in the targeted countries contributing to SDG 3. Regarding SDG 10, the increment in vaccine usage would help reduce the inequality between countries. The benefits derived from vaccines, taken for granted in developed countries and some LMICs, could be further generalized to all LIC and LMICs.

Furthermore, this research contributes to SDG 17. It is an example of collaboration between academia and organizations such as UNICEF toward a sustainable world.