

**A MULTI-OBJECTIVE ROBUST
OPTIMIZATION MODEL FOR VACCINE
SUPPLY CHAIN UNDER UNCERTAINTY**

BY

ABDERRAHMEN BOUCHENINE

A Thesis Presented to the
COLLEGE OF GRADUATE AND INTERDISCIPLINARY STUDIES

KING FAHD UNIVERSITY OF PETROLEUM & MINERALS

DHAHRAN, SAUDI ARABIA

In Partial Fulfillment of the
Requirements for the Degree of

MASTER OF SCIENCE

In

**INDUSTRIAL AND SYSTEMS
ENGINEERING**

MAY 2024

A MULTI-OBJECTIVE ROBUST
OPTIMIZATION MODEL FOR VACCINE
SUPPLY CHAIN UNDER UNCERTAINTY

BY

ABDERRAHMEN BOUCHENINE

A Thesis Presented to the
DEANSHIP OF GRADUATE STUDIES

In Partial Fulfillment of the Requirements
for the Degree of

MASTER OF SCIENCE

IN

INDUSTRIAL AND SYSTEMS ENGINEERING

KING FAHD UNIVERSITY
OF PETROLEUM & MINERALS

Dhahran, Saudi Arabia

MAY 2024

KING FAHD UNIVERSITY OF PETROLEUM & MINERALS
DHAHRAN 31261, SAUDI ARABIA

DEANSHIP OF GRADUATE STUDIES

This thesis, written by **ABDERRAHMEN BOUCHENINE** under the direction of his thesis adviser and approved by his thesis committee, has been presented to and accepted by the Dean of Graduate Studies, in partial fulfillment of the requirements for the degree of **MASTER OF SCIENCE IN INDUSTRIAL AND SYSTEMS ENGINEERING**.

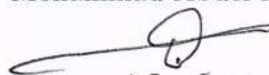
Thesis Committee



Dr. Ismail Almaraj (Adviser)



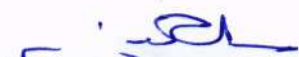
Dr. Mohammad Abdel-Aal (Member)



13-5-2024
Dr. Omar Alsawafy (Member)



Dr. Anas AlGhazi
Department Chairman



Dr. Suliman Al-Homidan
Dean of Graduate Studies

Date



©Abderrahmen Bouchenine
2024

Dedication

To the uncertain future.

ACKNOWLEDGMENTS

I would like to extend my deepest gratitude to Dr. Ismail Almaraj, for his invaluable guidance and mentorship throughout my Master thesis research. The insightful discussions, constructive feedback, and suggestions significantly enhanced the quality and rigor of this work. Furthermore, I wish to express my sincere appreciation to the esteemed committee members, Dr. Mohammad Abdel-Aal and Dr. Omar Alsawafy. Their comments and constructive feedback helped in refining the work significantly. I would like also to acknowledge the King Fahd University of Petroleum and Minerals for its support during this period by providing the platform to do my research. Last but not least, I owe my deepest gratitude to my guiding lights, my parents, whose love and support illuminate my path.

TABLE OF CONTENTS

ACKNOWLEDGMENTS	vi
LIST OF TABLES	x
LIST OF FIGURES	xi
LIST OF ABBREVIATIONS	xii
ABSTRACT (ENGLISH)	xiii
ABSTRACT (ARABIC)	xv
CHAPTER 1 INTRODUCTION	1
1.1 Vaccine Supply Chain Problems	2
1.2 Sustainable Supply Chain	4
1.3 Research Questions and Contributions	5
CHAPTER 2 LITERATURE REVIEW	7
2.1 Vaccine Supply Chain	7
2.2 Vaccine Waste Management	9
2.3 Optimization Under Uncertainty	10
CHAPTER 3 DESIGN AND OPTIMIZATION OF A ROBUST VAC- CINE SUPPLY CHAIN WITH DEFECTS AND WASTE UNDER MULTIPLE UNCERTAINTIES	14
3.1 Introduction	14

3.2	Problem Definition and Formulation	15
3.2.1	Notation	16
3.3	Robust Optimization	25
3.3.1	Definition	25
3.3.2	Combined Interval-Polyhedral Robust Counterpart Formulation	28
3.4	Solution Method	31
3.4.1	Lagrange Relaxation	31
3.4.2	Probabilistic guarantees of robust counterpart model	36
3.5	Computational Results	39
3.5.1	Performance of Lagrange Relaxation Algorithm	40
3.5.2	Sensitivity Analysis	41
3.6	Theoretical and Practical Implications	50
3.7	Conclusion	51

CHAPTER 4 A MULTI-OBJECTIVE ROBUST OPTIMIZATION MODEL WITH DEFECTIVE VACCINE AND REVERSE SUPPLY CHAIN UNDER UNCERTAINTY 54

4.1	Introduction	54
4.2	Model Description and Formulation	55
4.2.1	Notation	56
4.3	Solution Methodology	59
4.3.1	Robust optimization	59
4.3.2	Weighted Goal Programming Approach	59
4.4	Results and Discussion	61
4.4.1	Effect of Uncertainty	62
4.4.2	Weight Sensitivity Analysis	63
4.4.3	Sensitivity Analysis	64
4.5	Theoretical and Practical Implications	67
4.6	Conclusion	69

CHAPTER 5 CONCLUSION AND RECOMMENDATIONS	71
5.1 Work Summary	71
5.2 Future Research	72
APPENDIX A SENSITIVITY ANALYSIS : TABLE A.1	73
APPENDIX B SIZE OF PROBLEM 1 & 2 AND DATA INPUT	75
REFERENCES	77
VITAE	88

LIST OF TABLES

2.1	Review on related work.	13
3.1	Comparison of the different relaxed constraints.	32
3.2	Priori probabilistic bounds on constraint violation.	36
3.3	Gurobi vs. LRA performance.	40
3.4	Robust model with variation in Γ_D	45
3.5	Robust model with variation in $\Gamma_{\gamma_1, \gamma_2}$	45
3.6	Optimal set size Γ_i	46
3.7	Different bounds versus total cost.	53
4.1	Deterministic model results.	62
4.2	Results for the robust model with $\Gamma_i = J_i $	62
4.3	Weights combinations.	64
4.4	Sensitivity analysis to weights variations with $\Gamma_i = J_i $	65
A.1	Sensitivity analysis to parameters variation with $\Gamma_i = J_i $	74
B.1	Size of problem 1.3.	75
B.2	Size problem 2.4.	75
B.3	Input data	76

LIST OF FIGURES

3.1	Supply chain network for the proposed problem.	16
3.2	Combined interval-polyhedral uncertainty set illustration.	26
3.3	Lagrangian relaxation algorithm.	35
3.4	Objective function versus Γ_D	42
3.5	Objective function versus $\Gamma_{\gamma_1, \gamma_2}$	43
3.6	Probability bounds versus objective Function (instance 1).	48
3.7	Probability bounds versus objective Function (instance 3).	49
3.8	Probability bounds versus objective Function (instance 6).	49
4.1	Objective functions vs. weights.	66
4.2	Sensitivity analysis of the uncertain parameter.	68

LIST OF ABBREVIATIONS

GHG	greenhouse gas
LB	lower bound
LRA	Lagrange relaxation algorithm
MVSCN	multi-objective vaccine supply chain network
RO	robust optimization
SC	supply chain
UB	upper bound
VSCN	vaccine supply chain network
WHO	World Health Organization

THESIS ABSTRACT

NAME: Abderrahmen Bouchenine

TITLE OF STUDY: A MULTI-OBJECTIVE ROBUST OPTIMIZATION
MODEL FOR VACCINE SUPPLY CHAIN UNDER UN-
CERTAINTY

MAJOR FIELD: Industrial and Systems Engineering

DATE OF DEGREE: May 2024

The recent COVID-19 pandemic triggered a surge in concern on the global vaccine supply chain (SC), highlighting the critical need for improved vaccine access. This lack of access has significantly hampered efforts to eliminate the outbreak and achieve demand satisfaction. Most of the existing literature on vaccine SC builds assumptions upon perfect vaccine items with demand uncertainty. Nevertheless, frequently neglected imperfect and disrupted sustainable vaccine supply chain network (VSCN) under multiple uncertainties. Thus, it is important to consider vaccine defects and multiple uncertainties in the vaccine supply chain design.

In this thesis, we study first a VSCN with single objective. To address the uncertainty in the studied framework, a robust optimization (RO) approach is proposed to ensure

optimal vaccine distribution with less shortages, while a modified Lagrange relaxation algorithm (LRA) is presented to alleviate the computational burden of large-scale problems. Additionally, a priori probability bounds on constraint satisfaction are applied to guarantee demand fulfillment of healthcare centers with high probability and less total cost. We show the effectiveness of the VSCN model through a realistic illustrative example, the sensitivity analysis shows the efficacy and robustness of the proposed VSCN model compared to those in the literature by ensuring less shortages and better access to vaccine units allocated to the healthcare centers.

In the second half of this thesis, we study a multi-objective vaccine supply chain network under uncertainty based on the same assumptions introduced before. We consider a model that achieves sustainability by minimizing the overall cost of vaccine distribution, reducing greenhouse gas (GHG) emissions, and maximizing job opportunities within the network. To provide meaningful solutions that can withstand future parameter fluctuations, the robust optimization approach is employed to incorporate the decision-makers risk tolerance under a combined interval polyhedral set. In addition, the weighted goal programming approach is implemented to address the trade-off of the conflicting objectives of the proposed optimization problem. The results obtained from the illustrative example and sensitivity analysis show the efficacy of the proposed model.

ملخص الرسالة

الاسم: عبد الرحمن بوشنين

عنوان الدراسة: نموذج متين متعدد الاهداف لسلسلة امدادات اللقاح في ظل عدم اليقين

التخصص: الهندسة الصناعية والنظم

تاريخ الدرجة العلمية: مايو 2024

لقد أثارت جائحة كوفيد-19 التي تفشت مؤخرًا قلقًا متزايدًا بشأن سلسلة إمدادات (SC) اللقاحات عالميًا، مما يسلب الضوء على الحاجة الماسة إلى تحسين إمكانية الحصول عليها. وقد أعاق هذا النقص في الوصول إلى هذه اللقاحات إلى حد كبير الجهود المبذولة للقضاء على تفشي الوباء وتحقيق تلبية الطلب. وتبنى معظم الأدبيات الحالية حول سلسلة إمداد اللقاحات على افتراضات تستند إلى عناصر لقاح مثالية مع عشوائية الطلب. ومع ذلك، كثيرًا ما أهملت في كثير من الأحيان شبكة سلسلة الإمداد باللقاحات (VSCN) المعيبة لأسباب الجودة والمتعطلة أخذًا بالاعتبار حالات عدم اليقين المتعددة. وبالتالي، من المهم مراعاة عيوب اللقاح وأوجه عدم اليقين المتعددة في تصميم سلسلة إمداد اللقاحات. في هذه الأطروحة، ندرس أولاً (VSCN) بهدف واحد. ولمعالجة عدم اليقين في الإطار المدروس، يُقترح نهج التحسين القوي (RO) لضمان التوزيع الأمثل للقاح بتكلفة أقل، بينما يتم تقديم استرخاء لاغرانج (LRA) المعدل لتخفيف العبء الحسابي للمشاكل واسعة النطاق. بالإضافة إلى ذلك، يتم تطبيق حدود الاحتمالية المسبقة على استيفاء القيد لضمان تلبية الطلب لمراكز الرعاية الصحية باحتمالية عالية وتكلفة إجمالية أقل. تُظهر فعالية نموذج (VSCN) من خلال مثال توضيحي واقعي، ويُظهر تحليل الحساسية فعالية ومتانة نموذج (VSCN) المقترح مقارنةً بالنماذج الموجودة في الأدبيات من خلال ضمان تكلفة أقل ووصول أفضل إلى وحدات اللقاح المخصصة لمراكز الرعاية الصحية.

في النصف الثاني من هذه الأطروحة، ندرس شبكة سلسلة توريد لقاحات متعددة الأهداف في ظل حالة عدم اليقين بناءً على نفس الافتراضات المقدمة من قبل. وننظر في نموذج يحقق الاستدامة من خلال تقليل التكلفة الإجمالية لتوزيع اللقاحات إلى الحد الأدنى، وتقليل انبعاثات غازات

الاحتباس الحراري (GHG)، وتعظيم فرص العمل في النموذج المقترح. لتوفير حلول ذات مغزى يمكنها تحمل تقلبات المعلومات المستقبلية، يتم استخدام نهج التحسين القوي لدمج تحمل المخاطر لدى صانعي القرار. بالإضافة إلى ذلك، يتم تطبيق نهج برمجة الأهداف المرجحة لمعالجة المفاضلة بين الأهداف المتضاربة لمشكلة التحسين المقترحة. تُظهر النتائج التي تم الحصول عليها من المثال التوضيحي وتحليل الحساسية فعالية النموذج المقترح.

CHAPTER 1

INTRODUCTION

Supply chain management comprises three distinct decision-making levels: strategic, tactical, and operational. Strategic planning focuses on long-term objectives, encompassing the construction and/or location of sites, product development, system design, and customer identification. Tactical management tackles mid-term goals, including material procurement, production scheduling, and inventory management. Operational decisions, on the other hand, pertain to the day-to-day management of production processes and logistics activities. This thesis investigates problems relevant to both strategic and operational levels. Specifically, our approaches solve the following decision-making problems simultaneously: (1) Determine which supplier to select, and which facilities to open for each echelon and period, (2) decide on the optimal flow of quantities to distribute for both vaccine items and vaccine wastes, (3) and establish on the optimal inventory of vaccine waste to overcome the overflow in the opened vaccine waste storages.

1.1 Vaccine Supply Chain Problems

Over the past few decades, supply chains have experienced numerous disruptions. The COVID-19 pandemic, in particular, has profoundly transformed the global supply chain network, posing significant challenges for businesses, organizations, and most critically, healthcare systems. It brought about a significant downturn in the global economy, leading to a severe recession and widespread unemployment [1]. Consequently, the absence of clear guidelines for replicating supply chain disruptions and their impact on companies performance has heightened awareness among most firms of the severe and catastrophic consequences of this pandemic [2]

Immunization stands as a highly cost-effective strategy for curbing disease outbreaks, over the years, vaccination has proven to be the most efficient way to suppress and contain the dissemination of contagious diseases [3]. The COVID-19 pandemic, on the other hand, has had a profound impact on vaccine supply chains, leading to significant disruptions in recent years. This has presented formidable challenges for policymakers in effectively distributing vaccines, particularly in developing countries. Recognizing the urgency of this situation, the World Health Organization (WHO) has defined three critical priorities for containing epidemics through mass vaccination: ensuring a secure and reliable supply of high-quality vaccines and packaging materials; improving the efficiency and effectiveness of immunization supply systems; and minimizing the environmental footprint of immunization supply chains [4]. Recent research has extensively explored and addressed these preferences in the literature, seeking to overcome vaccine supply chain challenges across its entire life cycle. Particularly, four crucial

components of the vaccine supply chain have been the focus of attention: product, production, allocation, and distribution [4]. The distribution of vaccines poses a more complex task compared to the distribution of other medical supplies. Vaccine delivery entails multiple levels, spanning from the manufacturer to distribution centers and finally to medical facilities (hospitals, school/university medical centers). This intricate process has rendered mass vaccination planning a challenging endeavor for both researchers and practitioners [5]. Moreover, a substantial increase in medical waste generation from healthcare facilities during vaccination campaigns presents a major challenge in pandemic mitigation strategies. This hazardous waste demands appropriate management and disposal practices to avert environmental harm and protect public health [6]. Consequently, vaccine waste constitutes an additional threat that demands careful treatment and disposal procedures to protect both medical personnel and those engaged in containment initiatives [6].

Overall, the vaccine supply chain is vulnerable to disruptions arising from a multitude of factors. One of the major causes contributing to vaccine shortages and stockouts is the presence of defective or contaminated vials. Therefore, vaccine inspection may be conducted at various stages throughout the distribution process, culminating at the point of delivery to the end user. Furthermore, re-inspection of items is frequently required to guarantee the quality of vaccine batches delivered to customers, as contamination and defects may arise at various points within the supply. According to [7], two deaths were reported in August 2021 in Japan, after finding tiny black substances in vials from COVID-19 vaccine lots, however, the reason for death is still uncovered. After this incident, the pharmaceutical supplier and Japanese authorities

recalled three batches, totaling 1.63 million doses, on September 1st, 2021 [7]. This situation led to significant financial losses and a critical shortage of vaccine supply, resulting in stockouts. Investigations revealed that manufacturing errors were the predominant cause of contamination, with foreign substances and improperly inserted needles also contributing to the issue [8]. Given its critical significance in vaccine manufacturing and distribution, inspection demands meticulous attention. Accordingly, the current body of literature on vaccine quality control, inclusive of its waste management strategies, warrants further elaboration and expansion, as the integration of these concerns has received limited attention in existing research.

1.2 Sustainable Supply Chain

Supply chain decarbonization is expected to be a game changer for the impact of organizations' climate actions as per [9]. During the COVID-19 pandemic, many borders closed, which reduced the transportation and distribution of goods around the globe. As a result, the daily global CO₂ emissions decreased by 17% by April 2020, compared to 2019 [10]. This reflects the drastic impact of supply chain systems on carbon footprint emissions. Moreover, the United Nations climate change summit so-called COP26, which was held recently, has emphasized on low-carbon healthcare systems and their impact on the global sustainability and well-being of humankind. Therefore, building a sustainable and resilient vaccine SC is primordial for stakeholders and governments to create a net-zero VSCN system in the future.

When it comes to social aspects, a drastic loss of jobs has occurred due to the control-

ling measures and lockdowns in the last COVID-19 outbreak. Moreover, disruptions have cut down businesses for many organizations and firms. According to [11], the COVID-19 pandemic has triggered the worst job crises since the great depression. Experts and policymakers have raised their concerns about the long-term impact of this issue, which may turn into a social crisis. Therefore, revising the current situation and reconstructing a more resilient employment market is of high importance for future generations. Nevertheless, during epidemics such as COVID-19, many job opportunities could be created along the vaccine supply chains, bearing in mind the temporary situation of the outbreak, which makes job security a challenging task. Another issue that may arise during an outbreak is the spread of the virus and infections among workers, which may lead to the loss of skilled workers. Therefore, light should be shed on such scenarios to maintain social sustainability in the global SC.

1.3 Research Questions and Contributions

Despite the considerable progress in the state-of-the-art vaccine supply chain system design, the authors believe that each problem discusses the framework situation from different perspectives and the models developed to improve the underlying SC are still outstanding questions:

1. How do governments and healthcare providers ensure enough number of vaccine units to cope with the demand change?
2. Under the challenge of different sources of uncertainties, how would the robust decisions influence the SC configuration considering cost minimization and the

transported vaccine units across the supply chain?

3. What are the state-of-the-art techniques that could capture the lack of historical data of new epidemics in terms of vaccines and their waste along the supply chain?
4. How to design a sustainable vaccine supply chain taking into consideration the trade-off in economic, environmental, and social costs?

The rest of this thesis proceeds with the following structure. Chapter 2 reviews related literature on sustainable vaccine supply chains. Chapter 3 studies a robust optimization model for the vaccine supply chain under uncertainty with a single objective. Chapter 4 investigates a multi-objective robust optimization model for the vaccine supply chain under uncertainty. Finally, we conclude this thesis in Chapter 5.

CHAPTER 2

LITERATURE REVIEW

This chapter reviews relevant works on sustainable vaccine supply chain problems under uncertainty in different settings.

2.1 Vaccine Supply Chain

Since the appearance of the COVID-19 outbreak, many research has been conducted on the vaccine supply chain. For instance, the authors of [12] present a novel mathematical model for designing a sustainable SC for the COVID-19 vaccine, holistically integrating economic, environmental, and social factors to facilitate both domestic and international vaccine distribution. Furthermore, the authors introduced a robust data-driven model utilizing a polyhedral uncertainty set to effectively tackle the challenge of inequitable global vaccine distribution as an uncertain parameter. Building upon the work of reference [13], who develops a decision-support system for prioritizing vaccine distribution across an entire population, this study further refined the approach by employing predictive analysis for three distinct scenarios and segmenting the dis-

tribution chain into three phases. The optimized numerical outcomes generated from this refined approach provide healthcare authorities with enhanced decision-making capabilities for vaccine allocation strategies.

Plentiful aspects of vaccine distribution have been explored in the literature; the authors of [14] address the placement of COVID-19 vaccination facilities by proposing a data-driven approach to optimize vaccine distribution. The authors maintain that their proposed solution effectively addresses fairness concerns by mitigating the pandemic's death toll in multiple states without adversely affecting others. Additionally, the solution demonstrates remarkable resilience to uncertainties and forecast inaccuracies, sustaining comparable advantages across a diverse spectrum of perturbations. The reference [4] develops a framework for classifying the existing body of literature on vaccine logistics, aiming to bring order to this rapidly evolving field and identify potential areas for future research endeavors. They further identified several unique features of the vaccine supply chain, including substantial uncertainty in both supply and demand, conflicting objectives among different stakeholders, and decentralized decision-making structures. The authors of [15] formulate an inventory location optimization model to address the influenza vaccine supply chain in low-income countries during an outbreak. In [16], the authors develop a model for optimizing vaccine distribution to high-risk populations in a supply-constrained environment, this study further refined the approach by utilizing mobile vans to deliver vaccines to residents and staff across the United States and employing algorithms to optimize vaccine distribution strategies. The refined approach provides enhanced efficiency and effectiveness in vaccine delivery, ensuring equitable access to vaccines for vulnerable populations.

Leveraging a mathematical framework, the reference [17] develops an optimization vaccine distribution strategy that effectively caters to individuals with diverse priority levels, promoting equitable access to vaccinations. The authors of [18] present an in-depth analysis of the existing literature on vaccine distribution chains in developing countries. To address the challenges of efficient vaccine distribution during an outbreak. The reference [19] establishes a bi-objective non-linear programming queueing model for crisis vaccine supply chains. This model seeks to optimize two competing objectives: minimizing the average waiting time for vaccines and minimizing the total investment in vaccine holding and ordering. By considering the diverse needs of different population groups, this model ensures that vaccines are distributed in a timely and equitable manner. The authors of [20] construct a simulation model of the WHO’s program on the immunization supply chain in Benin, employing this model to examine the effects of using various primary vaccine containers for different vaccine antigens.

2.2 Vaccine Waste Management

Vaccine and medical waste as a high-priority and critical issue are one of the important aspects for any policymaker. Nevertheless, research in this field remains relatively underrepresented compared to other waste management areas, especially in the recent outbreak of COVID-19. In the following, a comprehensive review encompasses related papers on this subject. The authors of [21] construct a collaborative optimization model for the location and routing of infectious medical waste reverse logistics, in-

corporating economic and environmental perspectives. The reference [22] addresses a multi-objective multi-period mixed integer programming model for reverse logistics network design. This model seeks to identify the optimal locations for temporary waste treatment facilities and develop effective transportation strategies within a constrained time frame. The authors of [23] study a robust infectious medical waste reverse logistics network to curtail viral dissemination by developing a multi-objective linear programming model that minimizes overall costs and the risks associated with infectious medical waste transportation and treatment. The reference [24] establishes an efficacious medical waste transportation system to mitigate the transmission of COVID-19.

2.3 Optimization Under Uncertainty

Traditional models for vaccine supply chain network design typically assume uncertainty with a known probability distribution. In reality, this is rarely the case in outbreaks such as COVID-19. However, if someone can predict for instance the demand for vaccines using a probability distribution, a risk-neutral approach such as stochastic programming would be useful to develop a plan that minimizes the average overall cost [25]. Nevertheless, in most cases, the exact information on the distribution of the uncertain parameters is not available and it would be only known to lie within an uncertainty set. To deal with this uncertainty, a robust optimization approach would be the better choice. This approach makes sure the plan holds for all realizations within the uncertainty set range while minimizing the cost in the worst-

case scenario. The tractable robust counterpart problem is the resulting of RO which can be formulated for many different uncertainty sets [26]. The first RO optimization approach proposed was by [27] for linear optimization models which generate solutions within a box uncertainty set, though it provides conservative solutions. The authors of [28] propose later an ellipsoidal uncertainty set which significantly addresses the issue of conservatism, however, this approach leads to a nonlinear quadratic robust counterpart that is computationally expensive. While the reference [29] establishes an interval polyhedral uncertainty set approach that is less conservative with tractable computational complexity which is known in the literature as budget uncertainty set. When it comes the application of RO in VSCN, a substantial amount of papers has been discussed in the literature in the last three years during the outbreak of COVID-19. The authors of [30] focus on developing an efficient distribution of COVID-19 vaccines in Turkey’s provinces considering uncertainty in capacity and demand, this uncertainty is handled using a budget uncertainty set. The reference [31] builds a robust stochastic mathematical model to vaccinate the population with given priority while deciding on the location of distribution centers, inventory policies, and routing decisions to minimize the total cost. The authors of [32] propose a new way to design robust optimization supply chains that are both sustainable and resilient. They achieve this with a special mathematical model that considers two planning levels. Our extensive literature review is summarized in Table 2.1, presenting the most relevant research that have been carried out recently and how our work stands out from other published papers. Based on this review, our contribution can be summarized as follows.

- We address for the first time the design of a sustainable vaccine supply chain with defects under multiple uncertainties to guarantee model robustness taking into account, economic, environmental, and social costs.
- Develop a novel multi-objective, multi-period, and multi-vaccine SC model encompassing both vaccine distribution and waste management.
- Empower healthcare authorities with a systematic approach for informed decision-making and efficient execution.
- Incorporates stringent vaccine distribution and quality control requirements in the model while exploring alternative SC configurations and objectives optimization strategies which serves as a decision-making tool for efficient vaccine distribution and waste disposal across the SC network.
- Employ a RO technique to account for risk preferences and hedge against future parameter uncertainties.
- The proposed model presents itself from the existing literature by providing a valuable decision-support tool for supply chain managers in optimizing costs and ensuring optimal vaccine distribution with less shortages while achieving overall SC efficiency.

Authors	Defective vaccine items.	Sustainable vaccine SC	Vaccine waste.	Multi-vaccine SC	Multiple uncertainty	Uncertainty approach	Solution method
Chick et al. (2008) [33]	—	—	—	—	—	Deterministic	Game theory
Lee et al. (2011) [34]	—	—	—	*	—	Deterministic	Simulation approach
Sazvar, Z. et al. (2021) [32]	—	—	—	*	Demand	A robust optimization	Exact method
Manupati et al. (2021) [13]	—	—	—	—	Demand	predictive analysis	Decision Tree heuristic algorithm.
Gilani and Sahebi (2022) [12]	—	—	—	*	Demand	Polyhedral uncertainty	Cutting plane
Jahani et al. (2022) [19]	—	—	—	—	Demand	Queueing theory	Non-dominated SGA
Abbasi et al. (2023) [35]	—	—	*	—	—	Deterministic	Gray wolf optimizer.
Li et al. (2023) [36]	—	—	—	—	—	Deterministic	Game theory
Ensar Işık and Topaloglu Yildiz (2023) [30]	—	—	*	—	Demand Capacity	Robust optimization	Exact method
Kamran et al. (2023) [37]	—	—	—	*	—	Deterministic	Meta-heuristic
Habibi et al. (2023) [31]	—	—	—	—	—	Robust stochastic	Meta-heuristic
Rahman et al. (2023) [38]	—	—	—	*	—	chance-constrained	Genetic algorithm
This study	*	*	*	*	Demand,inspection vaccine waste treatment rate.	Robust optimization	Lagrange relaxation

Table 2.1: Review on related work.

CHAPTER 3

DESIGN AND OPTIMIZATION OF A ROBUST VACCINE SUPPLY CHAIN WITH DEFECTS AND WASTE UNDER MULTIPLE UNCERTAINTIES

3.1 Introduction

This chapter focuses on building a sustainable single-objective VSCN framework under multiple uncertainties where the vaccine items are considered imperfect. We address the formulation of this model using robust optimization, while a LRA is introduced as a solution methodology. Moreover, a prior bound on constraint violation is adopted

to generate less conservative solutions. The performance of the framework is assessed based on a numerical example.

3.2 Problem Definition and Formulation

In this work, we examine a vaccine supply chain system comprised of multiple periods, multi-products, and echelons. The flow of vaccines is illustrated in Figure 3.1 and can be described as follows: the vaccine orders are received from suppliers(s) to a set of healthcare distribution centers for inspection, and then moved to the healthcare centers according to the demand. Furthermore, due to the massive vaccination campaign, a considerable amount of vaccine waste is generated. Consequently, the vaccine wastes resulting from healthcare centers are shipped to vaccine waste storage centers along with defective items from the distribution centers. It is assumed that vaccine storage centers have an inventory in order to handle the substantial vaccine and medical waste generated from healthcare centers. Another reason for contemplating the inventory in the storage centers is that vaccine waste treatment centers have a defective treatment rate, which cannot treat all the generated vaccine waste directly due to machine breakdowns and periodic maintenance. Next, vaccine wastes are transported to potential treatment centers, these facilities in practice are dedicated to treating special medical waste generated from hospitals and clinics with special technology. Finally, the treated wastes are disposed of through landfills. The objective seeks to minimize the total cost of the supply chain network to better serve the healthcare centers with vaccine items and get dispose of vaccine waste generated in a proper manner.

The main assumptions taken into consideration in this framework are as follows: (1) all supply chain facilities are considered fixed and pre-defined, (2) healthcare distribution centers play a crucial role by inspecting and screening incoming vaccine orders for any defects, (3) the model accounts for the possibility of type I and II errors during inspection, treating them as uncertain parameters. In the following we provide the

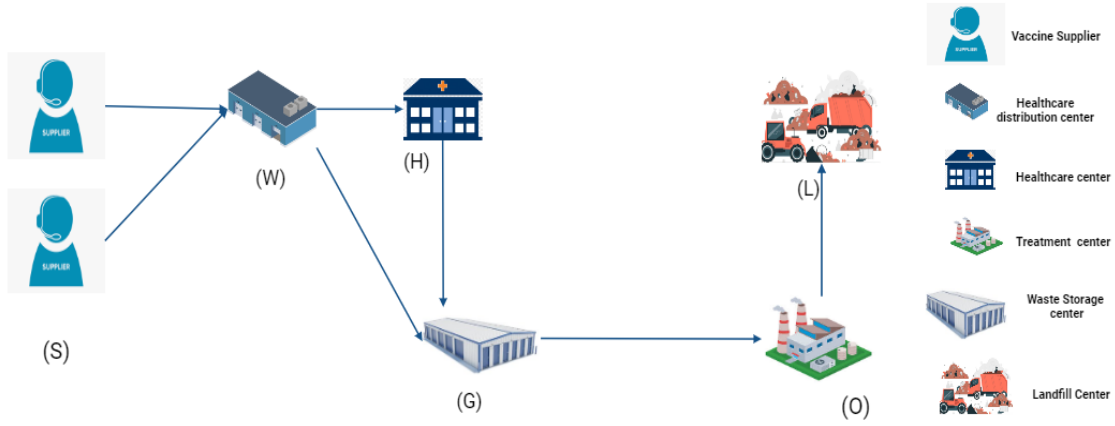


Figure 3.1: Supply chain network for the proposed problem.

necessary notation and introduce the deterministic formulation for the vaccine supply chain problem.

3.2.1 Notation

Sets

S : Set of possible suppliers $s \in S$.

W : Set of potential distribution centers $w \in W$.

H : Set of healthcare centers $h \in H$.

O : Set of potential treatment centers $o \in O$.

G : Set of potential storage centers $g \in G$.

L : Set of potential landfills $l \in L$.

P : Set of vaccine product types $p \in P$.

T : Set of time periods $t \in T$.

Uncertain Parameters

$\tilde{D}_{hpt}$: The demand of vaccine items $p \in P$ in the healthcare centers $h \in H$ at time t .

$\widetilde{VW}_{ht}$: The amount of vaccine waste generated in the healthcare centers $h \in H$ at time t .

$\tilde{\theta}_o$: The defective treatment rate in the potential treatment centers $o \in O$.

$\tilde{\gamma}_1$: Probability of type I error of inspection.

$\tilde{\gamma}_2$: Probability of type II error of inspection.

Parameters

FS_{st} : The fixed cost of supplier selection $s \in S$ at time t .

FW_{wt} : The fixed cost of opening a distribution center $w \in W$ at time t .

FG_{gt} : The fixed cost of opening vaccine waste storage center $g \in G$ at time t .

FO_{ot} : The fixed cost of opening a treatment center $o \in O$ at time t .

FL_{lt} : The fixed cost of opening a landfill $l \in L$ at time t .

D_{hpt} : The demand of vaccine items $p \in P$ in the healthcare centers $h \in H$ at time t .

VW_{ht} : The amount of vaccine waste generated in the healthcare centers $h \in H$ at time t .

KW_{wpt} : Ordering cost of vaccine items $p \in P$ incurred at the distribution center $w \in W$ at time t .

HCW_{wp} : The inventory holding cost of vaccine items $p \in P$ at the distribution center $w \in W$.

p_h : The shortage cost of vaccine items in the healthcare center $h \in H$.

c_{sp} : The purchasing cost per vaccine items $p \in P$ at the supplier $s \in S$.

HCG_g : The holding cost of vaccine waste in the waste storage centers $g \in G$.

TC_o : Treatment cost incurred in treatment center $o \in O$.

θ_o : The defective treatment rate in the potential treatment center $o \in O$.

I_{wp} : Inspection cost of the vaccine items $p \in P$ incurred at the distribution center $w \in W$.

p : The probability of defective items.

$(1 - p)$: The probability of non-defective items.

$\bar{p}$: The apparent probability of defective items.

$(1 - \bar{p})$: The apparent probability of non-defective items.

γ_1 : Probability of type I error of inspection.

γ_2 : Probability of type II error of inspection.

TS_{sw} : Transportation cost of vaccine items from potential suppliers $s \in S$ to distribution centers $w \in W$.

TW_{wh} : Transportation cost of vaccine from distribution centers $w \in W$ to healthcare centers $h \in H$.

TG_{wg} : Transportation cost of defective vaccine items from distribution centers $w \in W$ to waste storage center $g \in G$.

TH_{hg} : Transportation cost of vaccine waste from healthcare centers $h \in H$ to waste storage centers $g \in G$.

TM_{go} : Transportation cost of vaccine waste from the waste storage centers $g \in G$ to the treatment centers $o \in O$.

TO_{ol} : Transportation cost of treated vaccine waste from treatment centers $o \in O$ to landfills $l \in L$.

CS_{sp} : The capacity of supplier $s \in S$ vaccine $p \in P$.

CW_{wp} The capacity of distribution center $w \in W$ of vaccine $p \in P$.

CG_g : The waste storage center capacity $g \in G$.

CO_o : The treatment center capacity $o \in O$.

CL_l : The landfills capacity $l \in L$.

M : Big number.

Decision Variables

QS_{swpt} : Amount of vaccine $p \in P$ ordered from supplier $s \in S$ to distribution centers $w \in W$ at time t .

QW_{whpt} : Amount of vaccine $p \in P$ shipped from distribution centers $w \in W$ to healthcare centers $h \in H$ at time t .

QD_{wgpt} : Amount of defective vaccine $p \in P$ shipped from distribution centers $w \in W$ to vaccine waste storage center $g \in G$ at time t .

QU_{hpt} : Amount of unmet demand of vaccine items $p \in P$ to the healthcare center $h \in H$ at time t .

QH_{hgt} : Amount of vaccine waste shipped from healthcare centers $h \in H$ to vaccine waste storage centers $g \in G$ at time t .

QG_{got} : Amount of vaccine waste shipped from waste storage centers $g \in G$ to treatment facility $o \in O$ at time t .

QO_{olt} : Amount of treated vaccine waste shipped from treatment centers $o \in O$ to landfill $l \in L$ at time t .

INV_{gt} : Inventory level of vaccine waste at the waste storage center $g \in G$ at time t .

$Y_{wt}=1$: If an order is placed in the distribution center $w \in W$ at time t , and 0: otherwise.

$S_{st}=1$: If a supplier $s \in S$ is selected at time t , and 0: otherwise.

$W_{wt}=1$: If a distribution center $w \in W$ is opened at time t , and 0: otherwise.

$G_{gt}=1$: If storage center $g \in G$ is opened at time t , and 0: otherwise.

$O_{ot}=1$: If a treatment center $o \in O$ is opened at time t , and 0: otherwise.

$L_{lt}=1$: If landfill $l \in L$ is opened at time t , and 0 : otherwise.

Based on the introduced notation, the deterministic problem is formulated as follows.

Cost of opening potential facilities:

$$\begin{aligned} & \sum_{t \in T} \sum_{s \in S} FS_{st} \times S_{st} + \sum_{t \in T} \sum_{w \in W} FW_{wt} \times W_{wt} + \sum_{t \in T} \sum_{g \in G} FG_{gt} \times G_{gt} \\ & + \sum_{t \in T} \sum_{o \in O} FO_{ot} \times O_{ot} + \sum_{t \in T} \sum_{l \in L} FL_{lt} \times L_{lt} \end{aligned}$$

Transportation cost of vaccine items and generated wastes along the network:

$$\begin{aligned} & \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times TS_{swp} + \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QW_{whpt} \times (1 - \bar{p}) \times TW_{whp} \\ & + \sum_{t \in T} \sum_{h \in H} \sum_{g \in G} QH_{hgt} \times TH_{hg} + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times TM_{go} + \sum_{t \in T} \sum_{o \in O} \sum_{l \in L} QO_{olt} \times TO_{ol} \\ & + \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} QD_{wgpt} \times \bar{p} \times TG_{wg} \end{aligned}$$

Purchasing cost of vaccine items :

$$\sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times cS_{spt}$$

Configuration cost of the SC:

$$\begin{aligned}
& \sum_{t \in T} \sum_{w \in W} \sum_{p \in P} KW_{wpt} \times Y_{wt} + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times HCW_w \\
& + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times I_{wp} + \sum_{t \in T} \sum_{g \in G} INV_{gt} \times HCG_g + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times (1 - \tilde{\theta}_o) \times TC_o
\end{aligned}$$

Penalty cost:

$$\sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QU_{hpt} \times p_h$$

Our compact formulation for the proposed model is written as follows.

$$\begin{aligned}
Min \ Z = & \sum_{t \in T} \sum_{s \in S} FS_{st} \times S_{st} + \sum_{t \in T} \sum_{w \in W} FW_{wt} \times W_{wt} + \sum_{t \in T} \sum_{g \in G} FG_{gt} \times G_{gt} \\
& + \sum_{t \in T} \sum_{o \in O} FO_{ot} \times O_{ot} + \sum_{t \in T} \sum_{l \in L} FL_{lt} \times L_{lt} + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \\
& \times TS_{swp} + \sum_{t \in T} \sum_{w \in W} \sum_{p \in P} KW_{wpt} \times Y_{wt} + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \\
& \times cS_{spt} + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times I_{wp} + \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \\
& \times HCW_w + \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QW_{whpt} \times (1 - \bar{p}) \times TW_{whp} \\
& + \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QU_{hpt} \times p_h + \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} QD_{wgpt} \\
& \times \bar{p} \times TG_{wg} + \sum_{t \in T} \sum_{h \in H} \sum_{g \in G} QH_{hgt} \times TH_{hg} + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \\
& \times TM_{go} + \sum_{t \in T} \sum_{o \in O} \sum_{l \in L} QO_{olt} \times TO_{ol} + \sum_{t \in T} \sum_{g \in G} INV_{gt} \times HCG_g \\
& + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times (1 - \tilde{\theta}_o) \times TC_o
\end{aligned} \tag{3.1}$$

Subject to:

$$\sum_{s \in S} QS_{swpt} \times (1 - \bar{p}) \geq \sum_{h \in H} QW_{whpt} + \sum_{g \in G} QD_{wgpt} \times \bar{p} \quad \forall p, w, t \tag{3.2}$$

$$\sum_{w \in W} QW_{whpt} \times (1 - \bar{p}) + QU_{hpt} \geq \tilde{D}_{hpt} \quad \forall p, h, t \quad (3.3)$$

$$\sum_{w \in W} QS_{swpt} \leq CS_{sp} \times S_{st} \quad \forall p, s, t \quad (3.4)$$

$$\sum_{h \in H} QW_{whpt} \leq CW_{wp} \times W_{wt} \quad \forall p, w, t \quad (3.5)$$

$$\sum_{w \in W} QD_{wgpt} \times \bar{p} + \sum_{h \in H} QH_{hgt} \leq CG_g \times G_{gt} \quad \forall p, g, t \quad (3.6)$$

$$\sum_{g \in G} QG_{got} \times (1 - \tilde{\theta}_o) \leq CO_o \times O_{ot} \quad \forall o, t \quad (3.7)$$

$$\sum_{o \in O} QO_{olt} \leq CL_l \times L_{lt} \quad \forall l, t \quad (3.8)$$

$$\sum_{g \in G} QH_{hgt} = \widetilde{VW}_{ht} \quad \forall h, t \quad (3.9)$$

$$INV_{gt} = INV_{g(t-1)} + \sum_{w \in W} \sum_{p \in P} QD_{wgpt} \times \bar{p} + \sum_{h \in H} QH_{hgt} - \sum_{o \in O} QG_{got} \times (1 - \tilde{\theta}_o) \quad \forall g, t \quad (3.10)$$

$$INV_{gt} \leq CG_g \times G_{gt} \quad \forall g, t \quad (3.11)$$

$$\sum_{h \in H} QH_{hgt} + \sum_{w \in W} \sum_{p \in P} QD_{wgpt} \times \bar{p} \leq \sum_{o \in O} QG_{got} \quad \forall g, t \quad (3.12)$$

$$\sum_{g \in G} QG_{got} \times (1 - \tilde{\theta}_o) \leq \sum_{l \in L} QO_{olt} \quad \forall o, t \quad (3.13)$$

$$\sum_{s \in S} QS_{swpt} \leq M \times Y_{wt} \quad \forall p, w, t \quad (3.14)$$

$$\sum_{h \in H} QH_{hgt} \leq M \times G_{gt} \quad \forall g, t \quad (3.15)$$

$$S_{st}, W_{wt}, G_{gt}, O_{ot}, L_{lt}, Y_{wt} \in \{0, 1\} \quad \forall t \in T, s \in S, w \in W, g \in G, o \in O, l \in L. \quad (3.16)$$

$$QS_{swpt}, QW_{whpt}, QD_{wgpt}, QU_{hpt}, QH_{hgt}, QG_{got}, QO_{olt}, INV_{gt} \geq 0. \quad (3.17)$$

Equation (3.1) minimizes the total cost of the supply chain, constraint (3.2) states that the order amount of vaccine items from the supplier should be greater than the amount of perfect and defective vaccines shipped from the Healthcare distribution centers to healthcare centers and from distribution centers to vaccine waste storages respectively. Constraint (3.3) maintain the demand in the healthcare center, constraints (3.4), (3.5), (3.6), (3.7) and (3.8) are capacity limitations for the supplier, distribution centers, vaccine waste storages, vaccine waste treatment centers and landfills respectively. (3.9) Ensure that the vaccine waste generated in the healthcare centers is equal to the total amount of vaccine waste shipped to the storage center. (3.10) Represents the inventory balance at the vaccine waste storages, (3.11) limits the vaccine waste inventory to not exceed the storage center capacity, 3.12 is the flow balance of vaccine waste and defective vaccine items shipped from healthcare centers and distribution centers respectively to vaccine waste storages. (3.13) are the flow balance of vaccine wastes between treatment centers and landfills. (3.14) States that if an order is placed, a cost is incurred for each supplier. (3.15) Ensure the assignment of healthcare centers to the opened storage centers. (3.16) is a binary constraint, (3.17) is non-negativity constraints.

It is assumed that vaccine all vaccine units received from the supplier(s) are imperfect. Screening and inspection are performed in two stages; the first at the supplier level, and the second at the distribution centers. However, the inspection process is not perfect, and two types of errors can arise: type I error (γ_1) occurs when a conforming vaccine unit is misclassified as non-conforming, and type II error (γ_2) occurs when a non-conforming-vaccine-unit-is misclassified as conforming. The probability of under-

lying errors is constant in all distribution centers. If the proportion of defective units in a vaccine order is denoted as p , then the apparent non-defective items probability is obtained as follows.

$$(1 - p)(1 - \tilde{\gamma}_1) + p \times \tilde{\gamma}_2 = 1 - \tilde{\gamma}_1 - p(1 - \tilde{\gamma}_1 - \tilde{\gamma}_2) = 1 - \bar{p} \quad (3.18)$$

Where

$$\bar{p} = \tilde{\gamma}_1 + p(1 - \tilde{\gamma}_1 - \tilde{\gamma}_2) \quad (3.19)$$

The apparent probability of defective items.

$$p(1 - \tilde{\gamma}_2) + (1 - p)(\tilde{\gamma}_1) = p - p(\tilde{\gamma}_2) - p(\tilde{\gamma}_1) + \tilde{\gamma}_1 = \tilde{\gamma}_1 + p(1 - \tilde{\gamma}_1 - \tilde{\gamma}_2) = \bar{p} \quad (3.20)$$

In the proposed framework, the following four parameters are considered as uncertain:

- demand ($\tilde{D}_{hpt}$)
- inspection errors ($\tilde{\gamma}_1, \tilde{\gamma}_2$)
- vaccine waste ($\tilde{VW}$)
- defective treatment rate ($\tilde{\theta}_o$).

The source of parameter uncertainties is justified as follows: (1) the rapid spread of infections and severity of the outbreak leads to randomness in vaccine demand, (2) due to quality issues and miss-classification of vaccine items, inspection errors are considered uncertain, (3) massive vaccination campaign yields uncertainty in vaccine waste, and (4) because of machine breakdowns and scheduled maintenance,

treatment rate of infectious vaccine waste is considered uncertain. Additionally, due to the lack of expert judgment and historical data on these parameters, a robust optimization approach has been deployed to capture the uncertainty.

3.3 Robust Optimization

Robust optimization is a young research field that has been developed in the last two decades. RO is very practical since it is tailored to the information at hand, and it leads to computationally tractable formulations [39]. Different approaches have been discussed in the literature; the most well-known concepts are adjustable robust optimization which was introduced first in [28], while interval and budget uncertainty are coined by the authors of [29]. Our proposed model adopts the approach presented in [40], which provides the flexibility to choose the desired uncertainty set (combined interval-polyhedral) based on the decision-maker risk attitude.

3.3.1 Definition

By considering uncertainty in the deterministic model, the robust counterparts can be formulated by introducing the uncertain parameter within the desired uncertainty set. In the following, we show the combined interval-polyhedral robust counterpart formulation based on [40], Figure 3.2 shows the geometric theory behind RO in detail for both box and polyhedral uncertainty sets and its combination, where the perturbation of the parameters lie within the set size of the proposed interval-polyhedral

uncertainty set.

Let us consider the following deterministic linear optimization problem:

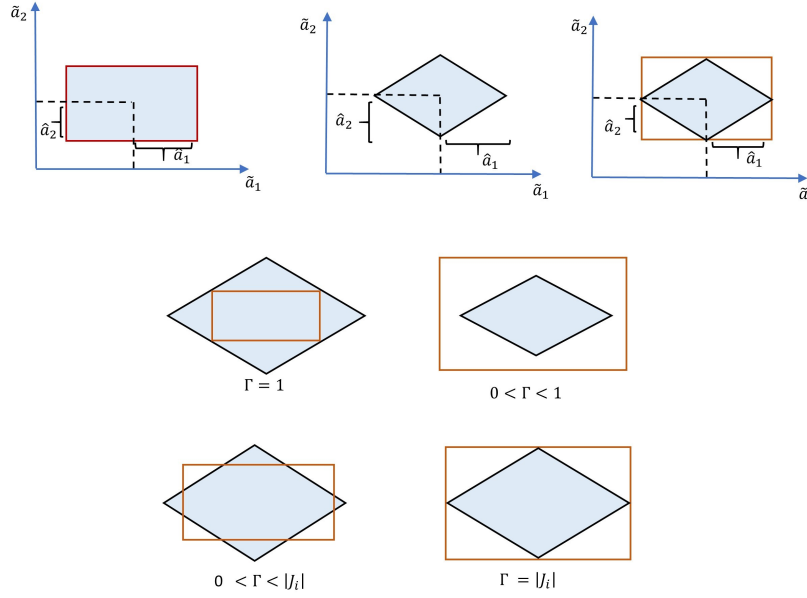


Figure 3.2: Combined interval-polyhedral uncertainty set illustration.

$$\text{Max } c^T x_j \quad (3.21)$$

$$\text{s.t. } Ax_j \leq b_j \quad (3.22)$$

$$x \in X \quad (3.23)$$

Where c^T , A , b_j and X are the n -vector of coefficients, $m \times n$ matrix of coefficients consumptions, m -vector of the right-hand-side values, and the uncertainty set of solutions.

Assume that c^T , $A(a_{ij})$ and b_j are uncertain parameters and considered bounded, symmetric, and independent. Then these parameters take the values in $[c_j - \hat{c}_j, c_j + \hat{c}_j]$, $[a_{ij} - \hat{a}_{ij}, a_{ij} + \hat{a}_{ij}]$ and $[b_j - \hat{b}_j, b_j + \hat{b}_j]$ where c_j , a_{ij} and b_j represent the nominal value of the parameters; $\hat{c}_j$ and $\hat{a}_{ij}$ represent the constant perturbation.

Then the equation can be rewritten as follows:

$$Max \sum_{j \in J} \tilde{c}_j x_j \quad (3.24)$$

$$s.t. \sum_{j \in J} \tilde{a}_{ij} x_j \leq \tilde{b}_j \quad \forall \quad i \in I \quad (3.25)$$

Where $\tilde{c}_j$, $\tilde{a}_{ij}$ and $\tilde{b}_j$ represent the true values which are subject to uncertainty.

Therefore, the above problem is formulated as follows:

$$Max \sum_{j \in J} c_j x_j + z_0 \Gamma_0 + \sum_{j \in J} p_{0j} \quad (3.26)$$

$$s.t. \sum_{j \in J} a_{ij} x_j + [z_i \Gamma_i + \sum_{j \in J} p_{ij} + p_{i0}] \leq b_j \quad \forall \quad i \in I \quad (3.27)$$

$$z_0 + p_{0j} \geq \hat{c}_j \quad \forall \quad j \in J_0 \quad (3.28)$$

$$z_i + p_{ij} \geq \hat{a}_j \quad \forall \quad j \in J_i \quad (3.29)$$

$$z_i + p_{i0} \geq \hat{b}_j \quad \forall \quad j \in J_i \quad (3.30)$$

$$z_0, z_i, p_{0j}, p_{ij}, p_{i0} \geq 0 \quad (3.31)$$

Where $z_0, z_i, p_{0j}, p_{ij}, p_{i0}$ are auxiliary variables, J_i denotes the index subset encompassing the variable indices corresponding to coefficients that are uncertain. Γ_i is the adjustable uncertainty set parameter for the combined interval-polyhedral uncertainty set.

3.3.2 Combined Interval-Polyhedral Robust Counterpart Formulation

The proposed model is formulated as a robust optimization problem with a combined interval-polyhedral uncertainty set, while the uncertainties in the objective function are taken into consideration by changing them into constraints; for the proof see [40]. The constraints containing uncertain parameters are replaced by their robust counterparts and then added to the deterministic model as follows.

$$W_1 - \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QW_{whpt} \times TW_{whp} \times (1 - \bar{p}) - \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} W_{whpt}^{\gamma_1, \gamma_2} \quad (3.32)$$

$$-\Gamma_{\gamma_1, \gamma_2} \times m_{\gamma_1, \gamma_2} \geq 0$$

$$W_2 - \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} QD_{wgpt} \times TG_{wg} \times (\bar{p}) + \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} W_{wgpt}^{\gamma_1, \gamma_2} \quad (3.33)$$

$$+\Gamma_{\gamma_1, \gamma_2} \times m_{\gamma_1, \gamma_2} \geq 0$$

$$m_{\gamma_1, \gamma_2} + W_{whpt}^{\gamma_1, \gamma_2} \geq \hat{p} \times QW_{whpt} \quad \forall \quad w, h, p, t \quad (3.34)$$

$$m_{\gamma_1, \gamma_2} + W_{wgpt}^{\gamma_1, \gamma_2} \geq \hat{p} \times QD_{wgpt} \quad \forall \quad w, g, p, t \quad (3.35)$$

$$m_{\gamma_1, \gamma_2}, W_{whpt}^{\gamma_1, \gamma_2}, W_{wgpt}^{\gamma_1, \gamma_2} \geq 0 \quad (3.36)$$

$$W_3 - \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times TC_o \times (1 - \theta_o) - \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} W_{got}^{\theta} - \Gamma_{\theta} \times m_{\theta} \geq 0 \quad (3.37)$$

$$m_{\theta} + W_{got}^{\theta} \geq \hat{\theta}_o \times QG_{got} \quad \forall \quad g, o, t \quad (3.38)$$

$$m_{\theta}, W_{got}^{\theta} \geq 0 \quad (3.39)$$

$$\sum_{s \in S} QS_{swpt} \times (1 - \bar{p}) - \sum_{s \in S} W_{swpt}^{\gamma^1, \gamma^2} - \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} \geq \sum_{h \in H} QW_{whpt} \quad (3.40)$$

$$+ \sum_{g \in G} QD_{wgpt} \times \bar{p} + \sum_{g \in G} W_{wgpt}^{\gamma^1, \gamma^2} + \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} \quad \forall \quad w, p, t$$

$$m_{\gamma^1, \gamma^2} + W_{swpt}^{\gamma^1, \gamma^2} \geq \hat{p} \times QS_{swpt} \quad \forall \quad s, w, p, t \quad (3.41)$$

$$m_{\gamma^1, \gamma^2} + W_{wgpt}^{\gamma^1, \gamma^2} \geq \hat{p} \times QD_{wgpt} \quad \forall \quad w, g, p, t \quad (3.42)$$

$$m_{\gamma^1, \gamma^2}, W_{swpt}^{\gamma^1, \gamma^2}, W_{wgpt}^{\gamma^1, \gamma^2} \geq 0 \quad (3.43)$$

$$\begin{aligned} \sum_{w \in W} QW_{whpt} \times (1 - \bar{p}) - \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} - \sum_{w \in W} W_{whpt}^{\gamma^1, \gamma^2} + W_{hpt}^D + \Gamma_D \times m_D \\ + QU_{hpt} \geq D_{hpt} \quad \forall \quad h, p, t \end{aligned} \quad (3.44)$$

$$m_{\gamma^1, \gamma^2} + W_{whpt}^{\gamma^1, \gamma^2} \geq \hat{p} \times QW_{whpt} \quad \forall \quad w, h, p, t \quad (3.45)$$

$$m_D + W_{hpt}^D \geq \hat{D}_{hpt} \quad \forall \quad h, p, t \quad (3.46)$$

$$m_{\gamma^1, \gamma^2}, m_D, W_{hpt}^D, W_{whpt}^{\gamma^1, \gamma^2} \geq 0 \quad (3.47)$$

$$\sum_{w \in W} QD_{wgpt} \times \bar{p} + \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} + \sum_{w \in W} W_{wgpt}^{\gamma^1, \gamma^2} + \sum_{h \in H} QH_{hgt} \leq CG_g \times G_{gt} \quad \forall \quad g, p, t \quad (3.48)$$

$$m_{\gamma^1, \gamma^2} + W_{wgpt}^{\gamma^1, \gamma^2} \geq \hat{p} \times QD_{wgpt} \quad \forall \quad w, g, p, t \quad (3.49)$$

$$m_{\gamma^1, \gamma^2}, W_{wgpt}^{\gamma^1, \gamma^2} \geq 0 \quad (3.50)$$

$$\sum_{g \in G} QG_{got} \times (1 - \theta_o) - \Gamma_\theta \times m_\theta - \sum_{g \in G} W_{got}^\theta \leq CO_o \times O_{ot} \quad \forall \quad o, t \quad (3.51)$$

$$m_\theta + W_{got}^\theta \geq \hat{\theta}_o \times QG_{got} \quad \forall \quad g, o, t \quad (3.52)$$

$$m_\theta, W_{got}^\theta \geq 0 \quad (3.53)$$

$$\sum_{g \in G} QH_{hgt} + W_{ht}^{VW} + \Gamma_{VW} \times m_{VW} = VW_{ht} \quad \forall h, t \quad (3.54)$$

$$m_{VW} + W_{ht}^{VW} \geq V\hat{W}_{ht} \quad \forall h, t \quad (3.55)$$

$$m_{VW}, W_{ht}^{VW} \geq 0 \quad (3.56)$$

$$INV_{gt} = INV_{g(t-1)} + \sum_{w \in W} \sum_{p \in P} QD_{wgpt} \times \bar{p} + \Gamma_{\gamma 1, \gamma 2} \times m_{\gamma 1, \gamma 2} + \sum_{w \in W} W_{wgpt}^{\gamma 1, \gamma 2} \quad (3.57)$$

$$+ \sum_{h \in H} QH_{hgt} - \sum_{o \in O} QG_{got} \times (1 - \theta_o) + \Gamma_{\theta} \times m_{\theta} + \sum_{o \in O} W_{got}^{\theta} \quad \forall g, p, t$$

$$m_{\gamma 1, \gamma 2} + W_{wgpt}^{\gamma 1, \gamma 2} \geq \hat{p} \times QD_{wgpt} \quad \forall w, g, p, t \quad (3.58)$$

$$m_{\theta} + W_{got}^{\theta} \geq \hat{\theta}_o \times QG_{got} \quad \forall g, o, t \quad (3.59)$$

$$m_{\theta}, m_{\gamma 1, \gamma 2}, W_{got}^{\theta}, W_{wgpt}^{\gamma 1, \gamma 2} \geq 0 \quad (3.60)$$

$$\begin{aligned} \sum_{h \in H} QH_{hgt} + \sum_{w \in W} \sum_{p \in P} QD_{wgpt} \times \hat{p} + \Gamma_{\gamma 1, \gamma 2} \times m_{\gamma 1, \gamma 1} + \sum_{w \in W} \sum_{p \in P} W_{wgpt}^{\gamma 1, \gamma 2} \\ \leq \sum_{o \in O} QG_{got} \quad \forall g, o, t \end{aligned} \quad (3.61)$$

$$m_{\gamma 1, \gamma 2} + W_{wgpt}^{\gamma 1, \gamma 2} \geq \hat{p} \times QD_{wgpt} \quad \forall w, g, p, t \quad (3.62)$$

$$m_{\gamma 1, \gamma 2}, W_{wgpt}^{\gamma 1, \gamma 2} \geq 0 \quad (3.63)$$

$$\sum_{g \in G} QG_{got} \times (1 - \theta_o) - \Gamma_{\theta} \times m_{\theta} - \sum_{g \in G} W_{got}^{\theta} \leq \sum_{l \in L} QO_{olt} \quad \forall o, t \quad (3.64)$$

$$m_{\theta} + W_{got}^{\theta} \geq \hat{\theta}_o \times QG_{got} \quad \forall g, o, t \quad (3.65)$$

$$m_{\theta}, W_{got}^{\theta} \geq 0 \quad \forall g, o, t \quad (3.66)$$

Constraints (3.4), (3.5), (3.8), (3.11), (3.14), (3.15), (3.16) and (3.17) remain the same as in the deterministic.

Where, $\Gamma_{\gamma 1, \gamma 2}, \Gamma_{\theta}, \Gamma_D, \Gamma_{VW}$ and $\hat{p}, \hat{\theta}, \hat{D}_{hpt}, V\hat{W}_{ht}$ are polyhedral adjustable uncertain parameters and parameter deviation from nominal values for inspection errors, treatment rate, demand, and vaccine waste respectively. Whereas $W_1, W_2, W_3, m_{\gamma 1, \gamma 2}, W_{whpt}^{\gamma 1, \gamma 2}, W_{wgpt}^{\gamma 1, \gamma 2}, W_{wspt}^{\gamma 1, \gamma 2}, m_{\theta}, W_{got}^{\theta}, W_{hgt}^{\theta}, m_D, W_{hpt}^D$ and m_{VW}, W_{ht}^{VW} are auxiliary variables.

3.4 Solution Method

In this section, we introduce a Lagrangian relaxation-based algorithm to address large-scale instances of the proposed framework. Furthermore, to account for the decision-maker's risk tolerance, this study establishes a priori bound on constraint violation within the robust counterpart model. This approach facilitates the generation of feasible and less conservative solutions compared to its rivals.

3.4.1 Lagrange Relaxation

Lagrangian relaxation has proven to be a powerful algorithmic tool for tackling large-scale mixed-integer linear programming problems. Its efficacy has been demonstrably validated through extensive literature, showcasing successful applications in optimizing diverse supply chain networks ([41], [42], [43]). The concept of Lagrangian relaxation, introduced by Geoffrion in the 1970s [44], hinges on the iterative update of Lagrangian multipliers associated with the relaxed complicating constraints. The

subgradient method is then utilized to derive a lower bound for the minimization problem or an upper bound for the maximization problem. The relaxed problem yields an optimal or near-optimal solution, which establishes a lower bound for the minimization problem. Conversely, the upper bound is typically determined heuristically through the fixation of specific binary variables. The algorithm iteratively improves these bounds until a predefined termination criterion is satisfied or the gap between the bounds vanishes. The subtle details of the algorithm are elaborated upon in the subsequent subsections.

Lower bound. To obtain a lower bound, the complicating constraints must be

Relaxed constraints	Gap %	CPU time (seconds)
40	6	938
41	10	634
54	20	1255
40-41	13	409
54-41	20.8	597
40-4-5	0.38	236
54-4-5	24	523

Table 3.1: Comparison of the different relaxed constraints.

relaxed. In our model, the optimal relaxation strategy involves relaxing constraints (3.4), (3.5), and (3.40) based on the results obtained from Table 3.1. This relaxation

yields a readily solvable master problem, presented as follows.

$$\begin{aligned}
\text{Minimize } Z + \sum_p \sum_s \sum_t \lambda_{pst} & \left(\sum_{w \in W} Q S_{swpt} - C S_{sp} \times S_{st} \right) \\
& + \sum_p \sum_w \sum_t \lambda_{pwt} \left(\sum_{h \in H} Q W_{whpt} - C W_{wp} \times W_{wt} \right) \\
& + \sum_w \sum_p \sum_t \lambda_{pwt} \left(\sum_{s \in S} Q S_{swpt} \times (1 - \bar{p}) - \sum_{s \in S} W_{swpt}^{\gamma^1, \gamma^2} \right. \\
& \quad - \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} - \sum_{h \in H} Q W_{whpt} - \sum_{g \in G} Q D_{wgpt} \times \bar{p} \\
& \quad \left. - \sum_{g \in G} W_{wgpt}^{\gamma^1, \gamma^2} + \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} \right)
\end{aligned} \tag{3.67}$$

subject to : (3.8), (3.11), (3.14), (3.15), (3.16), (3.17) and (3.32) to (3.39) and (3.41) to (3.66)

The corresponding multipliers are defined as :

$$\lambda_{spt}^{k+1} = \max \left(0, \lambda_{spt}^k + \text{step}^k \left(\sum_{w \in W} Q S_{swpt} - C S_{sp} \times S_{st} \right) \right) \forall s, p, t \tag{3.68}$$

$$\lambda_{pwt}^{k+1} = \max \left(0, \lambda_{pwt}^k + \text{step}^k \left(\sum_{h \in H} Q W_{whpt} - C W_{wp} \times W_{wt} \right) \right) \forall p, w, t \tag{3.69}$$

$$\begin{aligned}
\lambda_{wpt}^{k+1} = \max \left(0, \lambda_{wpt}^k + \text{step}^k \left(\sum_{s \in S} Q S_{swpt} \times (1 - \bar{p}) - \sum_{s \in S} W_{swpt}^{\gamma^1, \gamma^2} - \Gamma_{\gamma^1, \gamma^2} \right. \right. \\
\quad \times m_{\gamma^1, \gamma^2} - \sum_{h \in H} Q W_{whpt} - \sum_{g \in G} Q D_{wgpt} \times \bar{p} - \sum_{g \in G} W_{wgpt}^{\gamma^1, \gamma^2} \\
\quad \left. \left. + \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} \right) \right) \forall w, p, t
\end{aligned} \tag{3.70}$$

The step sizes for each relaxed constraint are detailed below.

$$step_{pst}^{k+1} = \frac{\delta^k(UB - LB)}{\sum_p \sum_s \sum_t (\sum_{w \in W} QS_{swpt} - CS_{sp} \times S_{st})^2} \quad (3.71)$$

$$step_{pwt}^{k+1} = \frac{\delta^k(UB - LB)}{\sum_p \sum_w \sum_t (\sum_{h \in H} QW_{whpt} - CW_{wp} \times W_{wt})^2} \quad (3.72)$$

$$step_{wpt}^{k+1} = \frac{\delta^k(UB - LB)}{\sum_w \sum_p \sum_t (\sum_{s \in S} QS_{swpt}(1 - \bar{p}) - \sum_s W_{swpt}^{\gamma^1, \gamma^2} - \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2} - \sum_h QW_{whpt} - \sum_g QD_{wgpt} \times \bar{p} - \sum_g W_{wgpt}^{\gamma^1, \gamma^2} + \Gamma_{\gamma^1, \gamma^2} \times m_{\gamma^1, \gamma^2})^2} \quad (3.73)$$

The upper bound (UB) and lower bound (LB) represent the optimal limits determined at each iteration of the algorithm. To enhance the algorithm's convergence during the k-th iteration, a parameter denoted as δ^k is introduced. Usually, δ^k is initialized with a value of 2 at the beginning of the iteration. After a specified number of iterations, if there is no improvement in the lower bound, δ^k is reduced by half.

An iterative approach utilizing Lagrange multipliers and the subgradient method is employed to update the lower and upper bounds. Equations (3.68), (3.69), and (3.70) correspond to the Lagrange multipliers associated with the relaxed constraints (3.4), (3.5), and (3.40), respectively. Equations (3.71), (3.72), and (3.73) represent the step sizes taken for each corresponding constraint.

Upper bound. The upper bound is obtained at each iteration of the Lagrangian algorithm as follows. If the lower bound solution is feasible to the original problem, then an upper bound is attained. In the case where the upper and lower bounds converge,

ALGORITHM 1: A MODIFIED LAGRANGIAN RELAXATION ALGORITHM

```
1  Input data : problem data, matrices, vectors, scalars
2  Begin
3    Initialize
4     $k, n, \varepsilon, \lambda_{spt}^{k+1}, \lambda_{pwt}^{k+1}, \lambda_{wpt}^{k+1}, Z_{LB}, Z_{UB}, \delta^k, \beta$ 
5    Repeat
6      Solve relaxed problem
7      if  $Z_{lb}^k > Z_{LB}$ 
8         $Z_{LB} \leftarrow Z_{lb}^k$ 
9         $n \leftarrow 0$ 
10     else
11        $n \leftarrow n + 1$ 
12       if  $n = N$ 
13          $\delta^k \leftarrow \beta \delta^k$ 
14       end
15     end
16     if  $\sum_w Q_{S_{wpt}} \leq CS_{sp} \times S_{st}$  and  $\sum_h Q_{W_{hpt}} \leq CW_{wp} \times W_{wt}$  and  $\sum_s Q_{S_{wpt}}(1 - \bar{p}) - \sum_s W_{swpt}^{Y_1, Y_2} - \Gamma_{Y_1, Y_2} \times m_{Y_1, Y_2}$ 
17        $\geq \sum_h Q_{W_{hpt}} + \sum_g Q_{D_{wgp}} \times \bar{p} + \sum_g W_{wgp}^{Y_1, Y_2} + \Gamma_{Y_1, Y_2} \times m_{Y_1, Y_2}$ 
18       Solve Z
19        $Z_{LB} = Z_{UB}$ 
20       Break
21     else
22       Fix the binary variables  $S_{st}$  and  $W_{wt}$ 
23       Solve Z
24       if  $Z_{ub}^k > Z_{UB}$ 
25          $Z_{LB} \leftarrow Z_{ub}^k$ 
26       end
27     end
28     if  $(Z_{UB} - Z_{LB})/Z_{UB} \leq \varepsilon$ 
29       Break
30     else
31        $\lambda_{spt}^{k+1}, \lambda_{pwt}^{k+1}, \lambda_{wpt}^{k+1}$  using eq(3.68), (3.69) and (3.70) respectively.
32        $step_{pst}^{k+1}, step_{pwt}^{k+1}, step_{wpt}^{k+1}$  using eq(3.71), (3.72) and (3.73) respectively.
33     end
34   end
```

Figure 3.3: Lagrangian relaxation algorithm.

it signifies that the algorithm has identified the optimal solution and can terminate. However, if the solution derived from solving the master problem is infeasible a feasible solution is acquired as follows. The optimal solution to the binary decision variables S_{st} and W_{wt} of the subproblem are fixed and assigned constant values. Subsequently, the original problem is minimized, and the resulting solution is feasible and provides an upper bound for the original problem. Figure 3.3 presents the pseudocode of the proposed Lagrangian relaxation algorithm.

3.4.2 Probabilistic guarantees of robust counterpart model

This section introduces a probability-based approach to enhance the existing RO framework. This approach aims to produce a less conservative optimal solution that incorporates different characteristics of uncertainty bounds, including bounded uncertainty with detailed probability distribution [45]. It specifically addresses the limitations of traditional robust optimization methods, which often lead to overly conservative solutions. This conservatism arises because traditional methods cannot accurately reflect the decision-maker’s risk tolerance for different uncertainties. The proposed approach addresses this issue by incorporating probability bounds on constraint violations. This allows for a more realistic and better choice of uncertainty sets. Ultimately, this leads to higher-quality solutions that are both feasible and closer to the true optimum. Table 3.2 summarizes the different a priori bounds considered in this work.

Label	Bound	Applicable robust counterpart	Assumption on uncertainty distribution
B1 [29]	$\exp(\frac{-\Delta^2}{2 J_i })$	IP, B, E, IE, P	Independent, symmetric, bounded
B2 [46]	$\exp(\min_{\theta>0}(-\theta\Delta + \sum_{j \in J_i} \ln E[e^{\theta\xi_j}]))$	IP, B, E, IE, P	Independent, symmetric known probability distribution function
B3 [47]	$\exp(\min_{\theta>0}(-\theta\Delta_i + \sum_{k \in K_i} \ln G_{ik}(\theta)))$	IP, B, E, IE, P	$\xi_{ij} \in [-1, 1]$, known bounds on $E[\xi_{ij}]$

Table 3.2: Priori probabilistic bounds on constraint violation.

The probability of the upper bound on constraint violation for the combined interval-

polyhedral uncertainty set can be represented by the following expression.

$$Pr\left\{\sum_j a_{ij}x_j + \sum_{j \in J_i} \xi_j \hat{a}_{ij}x_j > b_i\right\} \leq Pr\left\{\sum_{j \in J_i} \xi_j \delta_j > \Delta\right\} \quad (3.74)$$

Where the parameters Δ and δ are defined as follows. (for the proof see [45])

$$\Delta = \Gamma, 0 \leq \delta_j \leq 1, \forall j \in J_i \quad (3.75)$$

It is worth mentioning that the bound B1 proposed by [29] is applicable to the interval-polyhedral uncertainty set and can be extended to other types of sets. Equation (3.76) explicitly expresses the bound on constraint violation for a specific scenario. In this scenario, $\{\xi_j\}_{j \in J_i}$ is assumed to be independent and follows a bounded and symmetric probability distribution with support in the interval $[-1,1]$.

$$Pr\left\{\sum_j a_{ij}x_j + \sum_{j \in J_i} \xi_j \hat{a}_{ij}x_j > b_i\right\} \leq \exp\left(-\frac{\Delta^2}{2|J_i|}\right) \quad (3.76)$$

The complete expression of bound B2 introduced by [46], is given as follows.

$$Pr\left\{\sum_j a_{ij}x_j + \sum_{j \in J_i} \xi_j \hat{a}_{ij}x_j > b_i\right\} \leq \exp(\min_{\theta > 0}\{-\theta\Delta + \sum_{j \in J_i} \ln E[e^{\theta\xi_j}]\}) \quad (3.77)$$

The random variable $\{\xi_j\}_{j \in J_i}$ is assumed to be independent and subject to symmetric known probability distribution for both Eq. (3.77) and Eq. (3.78). $E[e^{\theta\xi_j}]$ represents the moment generating function.

The bound B3 proposed by [48] is defined below.

$$Pr \left\{ \sum_j a_{ij}x_j + \sum_{j \in J_i} \xi_j \hat{a}_{ij}x_j > b_i \right\} \leq \exp(\min_{\theta > 0} \{ -\theta \Delta_i + \sum_{k \in K_i} \ln G_{ik}(\theta) \}) \quad (3.78)$$

$G_{ik}(\theta) = \mu_{ij} + \sinh(\theta) + \cosh(\theta)$ and K_i contain the indices of the $\lceil \delta_i^1 \rceil$ largest μ_{ij} .

a_{ij} and μ_{ij} are chosen such that $|E[\xi_j]| \leq \mu_{ij}$ [48].

The term ϵ_i^{priori} is set before solving the model by the decision-maker, reflecting the probability of constraint violation in the optimal solution. To determine the predefined bounds in Table 3.2 for a particular Δ_i (the lowest possible value of the uncertainty set) Eq. 3.79 is introduced.

$$Pr \left\{ \sum_j a_{ij}x_j + \sum_{j \in J_i} \xi_j \hat{a}_{ij}x_j > b_i \right\} \leq \epsilon_i^{priori} \quad (3.79)$$

By setting a desired ϵ_i^{priori} the following problem is optimized to get the optimal size of Δ_i .

$$\begin{aligned} & Min_{\Delta_i} \Delta_i \\ & s.t \quad B(\Delta_i) \leq \epsilon_i^{priori} \\ & \Delta_i \geq 0 \end{aligned} \quad (3.80)$$

$B(\Delta_i)$ is a priori bound expression, bounds B1, B2, and B3 are solved based on the following problems given by Eq. (3.81), Eq. (3.82) and Eq. (3.83), respectively.

$$\begin{aligned}
& \text{Min}_{\Delta_i} \Delta_i \\
& s.t \quad \frac{-\Delta^2}{2|J_i|} \leq \ln(\epsilon_i^{priori}) \\
& \Delta_i \geq 0
\end{aligned} \tag{3.81}$$

$$\begin{aligned}
& \text{Min}_{\Delta_i} \Delta_i \\
& s.t \quad -\theta\Delta + \sum_{j \in J_i} \ln E[e^{\theta\xi_j}] \leq \ln(\epsilon_i^{priori}) \\
& \Delta_i \geq 0
\end{aligned} \tag{3.82}$$

$$\begin{aligned}
& \text{Min}_{\Delta_i} \Delta_i \\
& s.t \quad -\theta\Delta_i + \sum_{k \in K_i} \ln G_{ik}(\theta) \leq \ln(\epsilon_i^{priori}) \\
& \Delta_i \geq 0
\end{aligned} \tag{3.83}$$

Eq. (3.82) and Eq. (3.83) are nonlinear and nonconvex problems because of the bilinear term $\theta\Delta_i$.

3.5 Computational Results

In this section, we delve into the application of the proposed framework and test its effectiveness through the presented approaches. To achieve this comprehensive understanding, we conduct an extensive numerical analysis, this analysis relies on an illustrative example presented in Appendix B. Specifically, we assess how well

the robust optimization approach performs in conjunction with probabilistic a priori bounds on constraint violation. While the implementation of the model is conducted in Python 3.11.4 and solved using Gurobi 10.0 on a Laptop Core (TM) i7 with 16 GB of RAM and a 3.00 GHz processor.

3.5.1 Performance of Lagrange Relaxation Algorithm

A comparative analysis is conducted to evaluate the performance of the Lagrangian relaxation algorithm with respect to the Gurobi solver. Table 3.3 summarizes the results obtained from solving the proposed model. In general, it can be noticed that the solver exhibits superior performance in terms of solution time for small and medium-scale instances. However, for large-scale instances, the LRA demonstrates the ability to provide acceptable solutions within a reasonable CPU time compared to the solver. This observation highlights and validates the LRA's suitability of addressing large-scale problems.

Scale	Instances	Total cost			Solution time (s)	
		LRA	Gap %	Gurobi	LRA	Gurobi
Small	I_1	6.31711×10^7	0.38	6.34151×10^7	240	86
Medium	I_2	5.75040×10^7	2.14	5.87651×10^7	370	173
	I_3	6.51971×10^7	3.58	6.76197×10^7	500	785
Large	I_4	9.30280×10^7	4.05	9.72561×10^7	650	1200
	I_5	11.0493×10^7	5	11.644200×10^7	710	1440
	I_6	14.0053×10^7	1.5	—	740	>6500

Table 3.3: Gurobi vs. LRA performance.

3.5.2 Sensitivity Analysis

Supply chain models often perform sensitivity analysis to assess how variations in modeling parameters impact the overall performance of the supply chain. This study employs a combined interval-polyhedral uncertainty set approach along with a priori probability bounds on constraint violation to solve the proposed model. Our sensitivity analysis is conducted in two phases: 1) Analyzing the worst-case scenario for each uncertain parameter individually and for all uncertain parameters acting simultaneously, and 2) performing a comprehensive analysis to assess the model's performance under different probability bounds on constraint violation.

First, we examine the deterioration of the total cost by consolidating demand and inspection error uncertainties with defective treatment rate and vaccine waste random parameters simultaneously (Tables 3.4 and 3.5). Figure 3.4 and 3.5 illustrate the effect of incorporating these parameters on the total cost. It is noticeable that the objective function increases gradually as Γ_D and $\Gamma_{\gamma_1, \gamma_2}$ increase within the range $\Gamma_D \in [0, |J_j|]$ and $\Gamma_{\gamma_1, \gamma_2} \in [0, |J_j|]$, respectively. In general, by considering solely demand uncertainty the lowest worst-case total cost is observed. Conversely, considering multiple uncertainties simultaneously for all demand, treatment rate, and vaccine waste achieve the highest worst-case cost. Additionally, by taking into account only demand uncertainty (Table 3.4), the increment in the uncertain set size within the range $\Gamma_D \in [0, |J_j|]$ deteriorates the objective function gradually until it reaches a total cost of 9.97817×10^7 unit/year. On the other hand, consolidating the three uncertainties all together with $\Gamma_{VW} = |J_j|$, $\Gamma_\theta = |J_j|$ and $\Gamma_D \in [0, |J_j|]$ for vac-

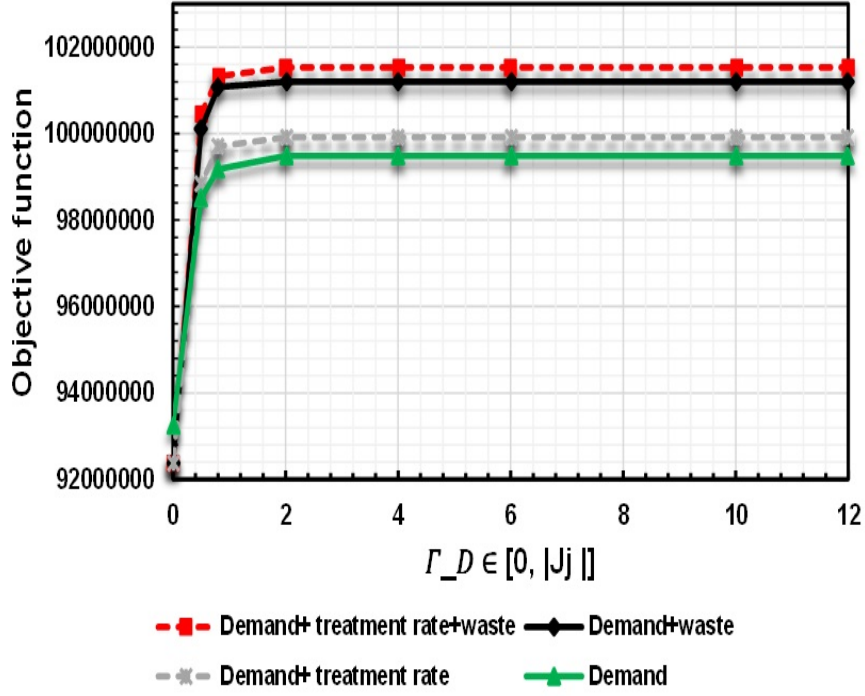


Figure 3.4: Objective function versus Γ_D .

cine waste, treatment rate and demand uncertainties respectively, achieve the highest worst-case scenario at $\Gamma_D = 2, \Gamma_{VW} = 12$ and $\Gamma_\theta = 5$ with an objective function of 10.1531×10^7 unit/year.

Figure 3.5 further illustrates the relationship between the uncertain set parameter of inspection errors and the total cost. It is evident that the objective function for type I and II errors exhibits the lowest value. On the other hand, combining all three uncertainties simultaneously attains the worst-case scenario total cost for all demand, defective treatment rate, and vaccine waste. When it comes to Table 3.5 an incremental increase is observed in the uncertain set size within the range $\Gamma_{\gamma_1, \gamma_1} \in [0, |J_j|]$ which increases the objective function gradually until it reaches the worst case at $\Gamma_{\gamma_1, \gamma_1} = 5$ with a total cost of 16.3286×10^7 unit/year. Contrary, incorporating all

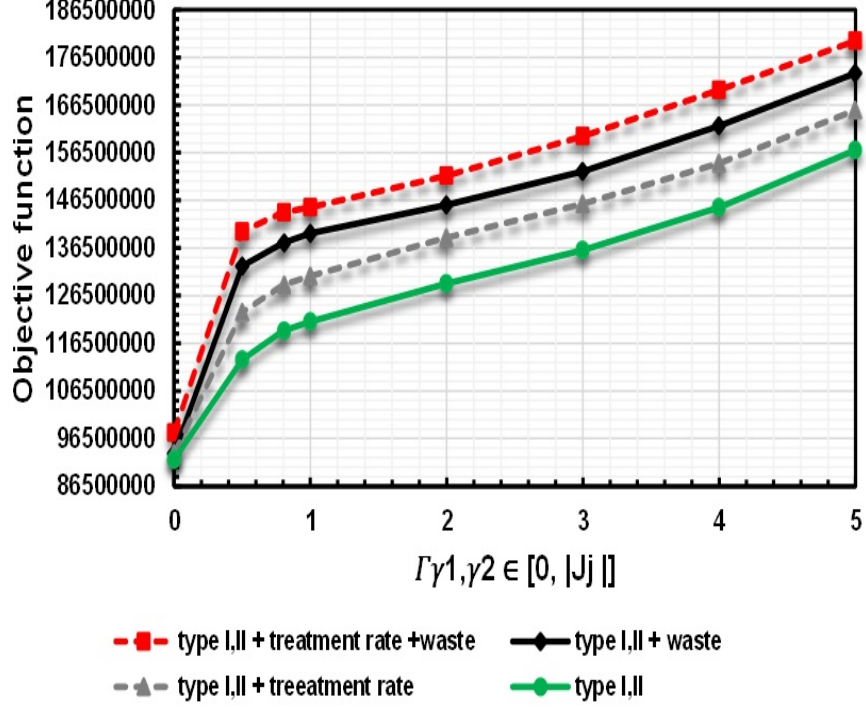


Figure 3.5: Objective function versus $\Gamma_{\gamma_1, \gamma_2}$.

three uncertainties together, $\Gamma_{\gamma_1, \gamma_1} \in [0, |J_j|]$, $\Gamma_{VW} = |J_j|$ and $\Gamma_{\theta} = |J_j|$ for inspection errors, vaccine waste, and treatment rate uncertainties respectively execute the highest worst-case scenario at $\Gamma_{\gamma_1, \gamma_2} = 5$, $\Gamma_{VW} = 12$ and $\Gamma_{\theta} = 5$ among all combinations studied with a total cost of 10.1531×10^7 unit/ year.

Overall, it can be concluded that consolidating multiple uncertainties gradually deteriorates the total cost and provides the decision-maker with greater flexibility and protection against any future parameter fluctuations. Conversely, disregarding a single uncertain parameter may result in suboptimality or infeasibility, which poses a significant challenge for policymakers in vaccine supply chain distribution and planning to manage uncertainties and hedge against shortages.

Based on the three probability bounds previously introduced, we aim in this subsection

to conduct a comprehensive analysis to assess the model's performance under different probability bounds on constraint violation. This analysis is undertaken to consider the decision-maker's risk aversion and provide a robust model with feasible solutions and reduced conservatism. First, the priori probability bounds B1, B2, and B3 are set. Next, the optimal set size is attained by optimizing equations (3.81), (3.82), and (3.83) for the three instances (I_1) , (I_3) and (I_6) , small, medium, and large problems. The uncertain parameters are presumed to be confined within a uniform probability distribution and exhibit bounded means, this implies for all $j \in J_i$, the random variable ξ_{ij} is independent and subject to a probability distribution supported on the bounded interval $[-1, 1]$, where $||E[\xi_j]|| \leq \mu_{ij}$ instead of $\tilde{a}_{ij}$ that yields $E[\xi_j] = 0$. Moreover, without loss of generality, the uncertain parameters can realize values with 10 % for inspection errors (γ_1, γ_2) and defective treatment rate (θ_o) , while the demand (D_{hpt}) and vaccine waste (VW_{ht}) are deviated with 15% of coefficient from nominal values. Thus, the bounded mean will be $||E[\xi_j]|| \leq 0.10$ for defective treatment rate and type I&II errors, while demand and vaccine waste means are set to $||E[\xi_j]|| \leq 0.15$.

Table 3.6 illustrates the optimal results obtained for different choices of Γ_i of each uncertainty set parameter as a function of the upper bounds of probability on constraint violation consistent with each problem instance (I_1) , (I_3) and (I_6) . A spectrum of probabilities ranging from 0.02 to 0.4 is analyzed to inform the decision-maker of the relationship between robustness and total cost. This analysis is conducted in recognition that total cost tends to increase as the level of conservatism increases. One major observation is the existence of a trade-off relationship between probability bounds and the set size of the uncertain parameters. As the a priori probability

Set size $\Gamma_D \in [0, J_j]$	Robust objective function	Set size $\Gamma_D \in [0, J_j]$ $\Gamma_{\theta= J_j }$	Robust objective function	Set size $\Gamma_D \in [0, J_j]$ $\Gamma_{VW= J_j }$	Robust objective function	Set size $\Gamma_D \in [0, J_j]$ $\Gamma_{\theta= J_j }$	Robust objective function
0	9.237×10^7	0	9.237×10^7	0	9.237×10^7	0	9.237×10^7
0.5	9.870×10^7	0.5	9.884×10^7	0.5	10.03×10^7	0.5	10.045×10^7
0.8	9.957×10^7	0.8	9.970×10^7	0.8	10.117×10^7	0.8	10.132×10^7
2	9.978×10^7	2	9.991×10^7	2	10.138×10^7	2	10.153×10^7
4	9.978×10^7	4	9.991×10^7	4	10.138×10^7	4	10.153×10^7
6	9.978×10^7	6	9.991×10^7	6	10.138×10^7	6	10.153×10^7
10	9.978×10^7	10	9.991×10^7	10	10.138×10^7	10	10.153×10^7
12	9.978×10^7	12	9.991×10^7	12	10.138×10^7	12	10.153×10^7

Table 3.4: Robust model with variation in Γ_D .

Set size $\Gamma_{\gamma_1, \gamma_2} \in [0, J_j]$	Robust objective function	Set size $\Gamma_{\gamma_1, \gamma_2} \in [0, J_j]$ $\Gamma_{\theta= J_j }$	Robust objective function	Set size $\Gamma_{\gamma_1, \gamma_2} \in [0, J_j]$ $\Gamma_{VW= J_j }$	Robust objective function	Set size $\Gamma_{\gamma_1, \gamma_2} \in [0, J_j]$ $\Gamma_{\theta= J_j }$	Robust objective function
0	9.237×10^7	0	9.237×10^7	0	9.237×10^7	0	9.237×10^7
0.5	12.08×10^7	0.5	12.10×10^7	0.5	12.24×10^7	0.5	12.26×10^7
0.8	12.55×10^7	0.8	12.57×10^7	0.8	12.71×10^7	0.8	12.73×10^7
1	12.74×10^7	1	12.76×10^7	1	12.90×10^7	1	12.92×10^7
2	13.35×10^7	2	13.36×10^7	2	12.90×10^7	2	13.52×10^7
3	14.06×10^7	3	14.07×10^7	3	14.21×10^7	3	14.23×10^7
4	15.02×10^7	4	15.03×10^7	4	14.21×10^7	4	15.18×10^7
5	16.32×10^7	5	16.34×10^7	5	16.47×10^7	5	16.49×10^7

Table 3.5: Robust model with variation in $\Gamma_{\gamma_1, \gamma_2}$.

bound increases, a corresponding decrease in set sizes is observed for all three bounds B1, B2, and B3. Notably, bound B2 consistently demonstrates the tightest set size with the lowest set sizes in Γ_D, Γ_{VW} equal to 2.68, 2.9, and 3.1, and the set sizes $\Gamma_{\theta}, \Gamma_{\gamma_1, \gamma_2}$ equal to 1.31, 1.5 and 1.72 for instances $(I_1), (I_3)$ and (I_6) respectively. In contrast, bound B3 consistently yields the most conservative set sizes, with the lowest set sizes of Γ_D, Γ_{VW} equal to 11.85, 13.5 and 15.42 and $\Gamma_{\theta}, \Gamma_{\gamma_1, \gamma_2}$ equal to 2.93, 3.89 and 4.84 for instances $(I_1), (I_3)$ and (I_6) respectively, while bound B1 falls between these two extremes, with its lowest set size of Γ_D, Γ_{VW} equal to 9.68, 10.46 and 11.18

and $\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$ equal to 2.34, 2.7 and 3.02 for instances $(I_1), (I_3)$ and (I_6) respectively.

It is worth mentioning that all set size instances are set with a priori probability bound of $\epsilon_i^{priori} = 0.4$.

Furthermore, the problem is systematically resolved for different values of the uncertain set parameters, thereby empowering the decision-maker with an improved choice of Γ_i characterized by meaningful and less conservative solutions. Table 10 illustrates the total cost associated with the three instances $(I_1), (I_3)$ and (I_6) as a function of a priori probability bound on constraint violation. An initial assessment of the three proposed probability bounds demonstrates that bound B2 consistently exhibits superior performance in terms of total cost and price of robustness across all three instance scales. It consistently manifests the lowest values for all constraint violation proba-

	ϵ_i^{priori}	Bound B1			Bound B2			Bound B3		
		I_1	I_2	I_6	I_1	I_2	I_6	I_1	I_2	I_6
Γ_D, Γ_{VW}	0.02	9.68	10.46	11.18	5.4	5.87	6.29	11.8	13.72	15.64
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		4.84	5.59	6.25	2.57	2.94	3.31	3.15	4.11	5.06
Γ_D, Γ_{VW}	0.05	8.74	9.15	9.79	4.77	5.17	5.54	11.73	13.65	15.57
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		4.23	4.89	5.47	2.23	2.6	2.96	3.08	4.04	5
Γ_D, Γ_{VW}	0.1	7.43	8.02	8.58	4.2	4.55	4.88	11.68	13.6	15.52
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		3.71	4.29	4.79	1.97	2.32	2.63	3.03	3.99	4.95
Γ_D, Γ_{VW}	0.2	6.21	6.71	7.17	3.53	3.82	4.1	11.63	13.55	15.47
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		3.1	3.58	4.01	1.69	1.98	2.23	2.98	3.94	4.9
Γ_D, Γ_{VW}	0.3	5.37	5.8	6.20	3.07	3.32	3.55	11.6	13.52	15.44
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		2.68	3.1	3.46	1.48	1.73	1.95	2.95	3.91	4.87
Γ_D, Γ_{VW}	0.4	4.68	5.06	5.41	2.68	2.9	3.1	11.58	13.5	15.42
$\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$		2.34	2.7	3.02	1.31	1.52	1.71	2.93	3.89	4.84

Table 3.6: Optimal set size Γ_i .

bilities, establishing itself as the most cost-effective and robust choice. Conversely, bounds B1 and B3 consistently report the highest total cost and price of robustness, indicating a less favorable trade-off between cost and robustness. More precisely, bound

B2 is the tightest bound with 39.7%, 52.49% and 56.95% of prices of robustness for the three instances $(I_1), (I_3)$ and (I_6) respectively. On the other hand, it can be noticed that bounds B1 and B3 have the worst-case objective function with 40% of constraint violation reporting a price of robustness of (65.91%, 50.68%), (87.54%, 69.57%) and (125.1%, 95.9%) for instances $(I_1), (I_3)$ and (I_6) respectively.

An apparent distinct tradeoff between the a priori probability bound on constraint violation and the total cost is noticed. Therefore, if the decision-maker chooses to accept only 2% probability of constraint violation with bound B2, then he/she has to select Γ_D, Γ_{VW} equal to 2.68, 2.9 and 3.1 and choose $\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$ equal to 1.31, 1.5 and 1.72, paying a price of robustness of 47.44%, 60.47% and 70.82% greater than the deterministic model. Whereas, if he/she accepts up to 40 % of probability of constraint violation for bound B2, then he/she has to choose Γ_D, Γ_{VW} equal to 2.68, 2.9 and 3.1 and pick $\Gamma_\theta, \Gamma_{\gamma_1, \gamma_2}$ equal to 1.31, 1.5 and 1.72, paying a price of robustness of 39.7%, 52.49% and 56.95% more than its deterministic model, which is less conservative than the previously mentioned.

To illustrate further the behavior of total cost as a function of priori probability bounds on constraint violation for the three bounds B1, B2, and B3, the obtained results from Table 3.7 are represented in Figures 3.6, 3.7, and 3.8. As a primary observation, bound B2 consistently demonstrates the lowest total cost among the three bounds for all three instances studied. Conversely, an overlap between bounds B1 and B3 is noticed in terms of the overall cost, suggesting that both bounds are more conservative compared to B2. However, no definitive conclusion can be drawn regarding which bound B1 or B3 is tighter.

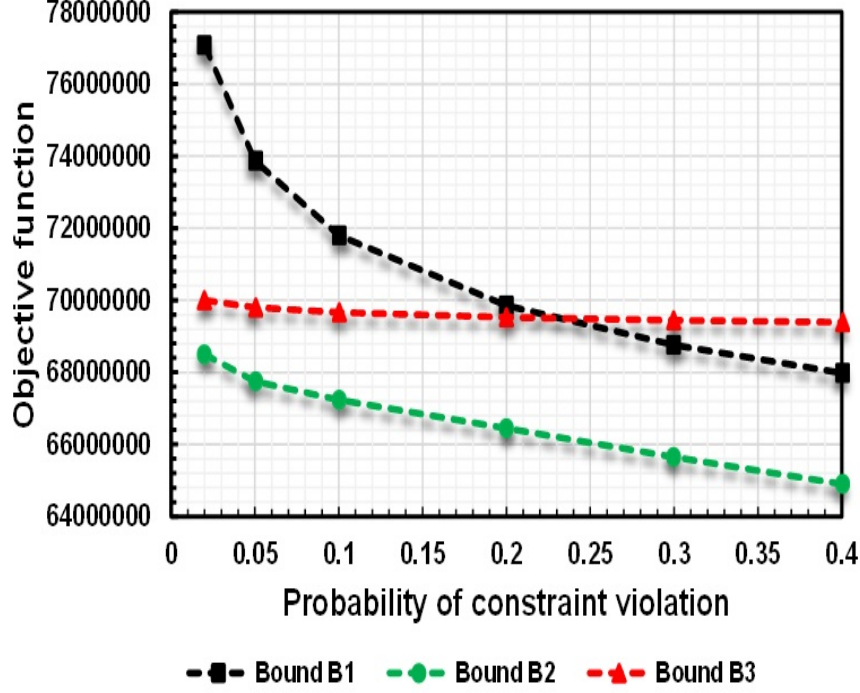


Figure 3.6: Probability bounds versus objective Function (instance 1).

It is worth mentioning that bound B2 consistently achieves the lowest total cost and price of robustness across all probability violations introduced, ranging from 0.02 to 0.4. If the decision-maker is willing to accept only a 2% probability of constraint violation, the worst-case scenario would result in total costs of 6.84958×10^7 , 7.41051×10^7 and 15.779×10^7 for the three instances (I_1) , (I_3) and (I_6) respectively. On the other hand, if the decision-maker accepts up to 40% probability of constraint violation, the total costs would be 6.48984×10^7 , 7.04202×10^7 and 14.4979×10^7 . Upon analyzing bounds B1 and B2, it is evident that for a 2% constraint violation probability, bound B1 manifests its worst-case scenario with total costs of 7.70773×10^7 , 8.66062×10^7 and 20.793×10^7 . Similarly, bound B3 achieves its worst-case scenario with total costs of 7.00001×10^7 , 7.83051×10^7 and 18.0959×10^7 for the three instances (I_1) , (I_3) and (I_6) .

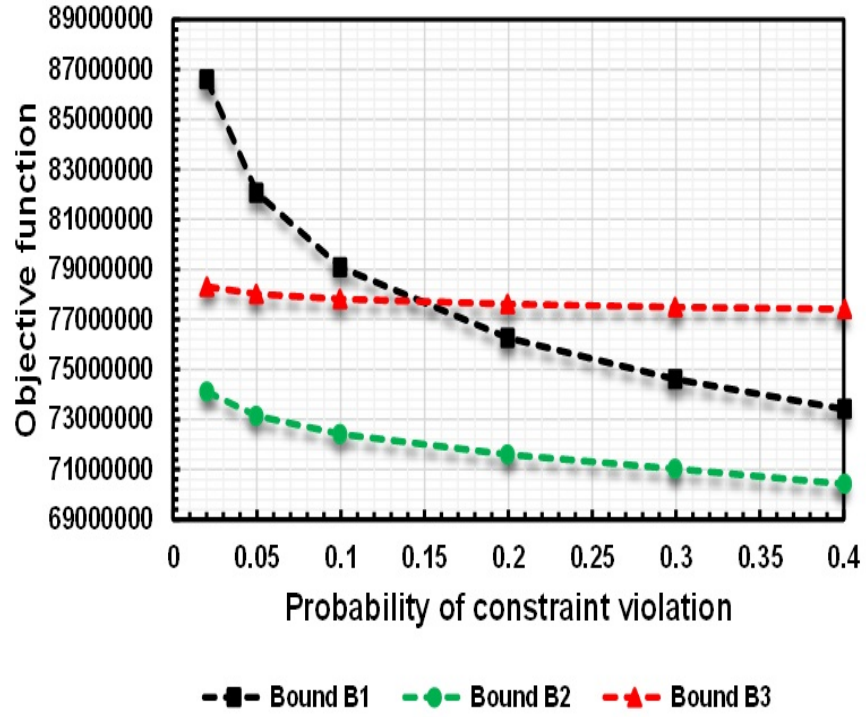


Figure 3.7: Probability bounds versus objective Function (instance 3).

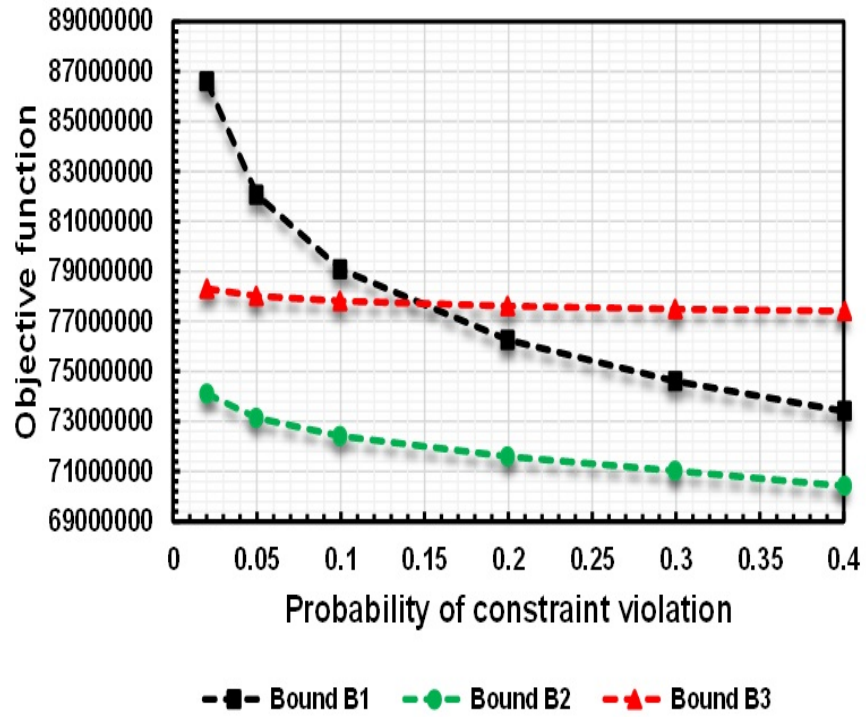


Figure 3.8: Probability bounds versus objective Function (instance 6).

respectively. This observation indicates that bound B1 exhibits a more conservative nature in this case. Additionally, if the decision-maker is willing to accept up to 40% constraint violation probability, the total cost associated with bound B1 becomes 6.79812×10^7 , 7.34151×10^7 and 15.502×10^7 which is less conservative compared to the results reported by bound B3 for the same constraint violation probability.

Overall, a clear tradeoff exists among the degree of conservatism and a priori probability bounds for the three bounds. This tradeoff manifests in an inverse relationship between the probability of constraint violation and the total cost. In other words, as the probability of constraint violation increases, the total cost decreases, and vice-versa.

3.6 Theoretical and Practical Implications

Decision-makers can leverage the introduced probability bounds to enhance their flexibility in selecting the appropriate uncertainty set size, effectively mitigating the risk of overly conservative solutions and total cost. This entails minimizing the size of the uncertainty set, as larger sets lead to more conservative solutions and consequently higher total costs in minimization problems. However, if the decision-maker exhibits a high-risk tolerance, they may choose to hedge against future parameter fluctuations by opting for a larger uncertainty set size. This trade-off is exemplified in vaccine supply chain management, where a severe and rapid outbreak could spread rapidly and impact the community. In such scenarios, policymakers must strike a balance between risk-averse and risk-tolerant strategies. Our proposed approach empowers

decision-makers to carefully select the desired set size with tighter probability bounds, protecting against future parameter deviations without incurring the risk of excessive conservatism. The proposed model aims to enhance VSCN productivity by optimizing the sourcing of vaccine items and their distribution along the network. In addition, it enables policymakers to optimize vaccine distribution efficiency, ensuring demand fulfillment, minimizing shortages, combating the spread of disease, and effectively managing infectious waste generated from large-scale vaccination campaigns.

3.7 Conclusion

Recent disruptions in the vaccine supply chain caused by outbreaks, natural disasters, and geopolitical conflicts, have highlighted critical challenges for policymakers. These disruptions limit access to vaccines for vulnerable communities. Additionally, the surge in vaccine demand and resulting waste from mass vaccination campaigns create significant burdens for practitioners. Consequently, designing a sustainable vaccine supply chain is paramount to ensure equitable access and minimize waste.

This manuscript contributes to the existing literature by proposing a novel mixed-integer linear programming model for a strategic and operational multi-vaccine, multi-period supply chain under uncertainty and quality inspection. The objective seeks to facilitate access to different types of vaccines during outbreaks and effectively manage infectious waste generated from mass vaccination campaigns while minimizing the total cost. The proposed model incorporates the decision-maker's risk attitude by providing robust and feasible solutions within acceptable computational time in the

presence of multiple uncertainties such as inspection errors, demand, vaccine waste, and defective treatment rates, which fall within a combined interval-polyhedral uncertainty set. A Lagrangian relaxation algorithm is proposed to address the computational complexity of large-scale instances. Additionally, different priori probability bounds on constraint violation have been drawn from the literature to account for the decision-makers risk behavior, offering flexibility and a better selection of the uncertainty set size Γ_i .

Overall, the model performance is shown through a realistic numerical example. Our results demonstrate that the robust optimization approach, combined with prior probability bounds on constraint violation has been successful in achieving the following: 1) Generating feasible solutions with a high probability of demand satisfaction, less shortages, and reduced cost, even under future parameter fluctuations. This translates to a less conservative approach, 2) providing valuable insights for healthcare decision-makers in building a resilient and robust VSCN under multiple uncertainties, and (3 showing the model sensitivity and behavior against parameter deviation.

	Small problem I_1					
ϵ_i^{priori}	Bound B1		Bound B2		Bound B3	
	Objective function	Price of robustness %	Objective function	Price of robustness %	Objective function	Price of robustness %
0.02	7.70×10^7	65.91	6.84×10^7	47.44	7×10^7	50.68
0.05	7.38×10^7	59	6.77×10^7	45.83	6.98×10^7	50.25
0.1	7.179×10^7	54.55	6.72×10^7	44.72	6.96×10^7	49.95
0.2	6.98×10^7	50.37	6.64×10^7	43.03	6.95×10^7	49.66
0.3	6.87×10^7	48	6.56×10^7	41.32	6.94×10^7	49.48
0.4	6.79×10^7	46.33	6.48×10^7	39.7	6.93×10^7	49.37
	Small problem I_3					
ϵ_i^{priori}	Bound B1		Bound B2		Bound B3	
	Objective function	Price of robustness %	Objective function	Price of robustness %	Objective function	Price of robustness %
0.02	8.66×10^7	87.54	7.41×10^7	60.47	7.83×10^7	69.57
0.05	8.2×10^7	77.7	7.31×10^7	58.38	7.8×10^7	68.94
0.1	7.9×10^7	71.25	7.24×10^7	56.81	7.78×10^7	68.5
0.2	7.62×10^7	65.11	7.15×10^7	55.02	7.76×10^7	68.08
0.3	7.46×10^7	61.56	7.1×10^7	53.80	7.74×10^7	67.82
0.4	7.34×10^7	58.98	7.04×10^7	52.49	7.74×10^7	67.65
	Small problem I_6					
ϵ_i^{priori}	Bound B1		Bound B2		Bound B3	
	Objective function	Price of robustness %	Objective function	Price of robustness %	Objective function	Price of robustness %
0.02	20.79×10^7	125.1	15.77×10^7	70.82	18.09×10^7	95.9
0.05	18.87×10^7	104.34	15.44×10^7	67.23	17.99×10^7	94.77
0.1	17.64×10^7	91	15.16×10^7	64.19	17.9×10^7	93.84
0.2	16.55×10^7	79.19	14.85×10^7	60.84	17.82×10^7	93.84
0.3	15.93×10^7	72.47	14.66×10^7	58.71	17.77×10^7	92.4
0.4	15.5×10^7	67.82	14.49×10^7	56.95	17.72×10^7	91.87

Table 3.7: Different bounds versus total cost.

CHAPTER 4

A MULTI-OBJECTIVE ROBUST OPTIMIZATION MODEL WITH DEFECTIVE VACCINE AND REVERSE SUPPLY CHAIN UNDER UNCERTAINTY

4.1 Introduction

In this chapter, we design a sustainable system for managing a multi-objective vaccine supply chain network (MVSCN) under multiple sources of uncertainties. We account for the fact that some vaccines might be imperfect (spoiled or ineffective). A robust optimization approach and goal programming method are introduced to handle un-

certainties and multi-objectiveness in the model, respectively. The performance of the proposed framework is demonstrated through an illustrative example.

4.2 Model Description and Formulation

We explore a multi-objective and multi-echelon vaccine supply chain network with different time periods and products. Figure 3.1 depicts the vaccine flow, starting with orders received from suppliers to the healthcare distribution centers for inspection. Subsequently, vaccines are transported to healthcare centers based on demand. A key aspect of the model is the substantial vaccine waste generation due to a massive vaccination campaign. Vaccine waste from healthcare centers, along with defective items from distribution centers, are transported to storage centers equipped with inventory management to handle the large volume of waste and avoid overflows. The need for storage also stems from the existence of defective treatment rates at dedicated vaccine waste treatment centers, where machine breakdowns and maintenance prevent immediate processing of all generated waste. Following storage, vaccines are transported to treatment facilities. The treated waste is then disposed of in landfills. The main assumptions taken into consideration for the proposed framework are as follows: (1) all supply chain facilities are considered fixed and pre-defined, (2) healthcare distribution centers play a crucial role by inspecting and screening incoming vaccine orders for any defects, (3) the model accounts for the possibility of type I and II errors (γ_1 and γ_2) during inspection, treating them as uncertain parameters. The optimization objective minimizes simultaneously the total cost, and carbon emissions and maximizes the

number of jobs created in the specified facilities due to the SC configuration aiming to efficiently serve healthcare centers with vaccines and manage generated waste disposal while accounting for environmental and social aspects.

4.2.1 Notation

The same notation as in Chapter 3 is utilized in this subsection, additional notations are introduced below.

Sets

I : Set of goals $i \in I$.

Environmental parameters

EES_{sw} : GHG emissions per unit of transported vaccine between supplier $s \in S$ and warehouse $w \in W$.

EEW_{wh} : GHG emissions per unit of transported vaccine between warehouse $w \in W$ and healthcare center $h \in H$.

EED_{wg} : GHG emissions per unit of transported defective vaccine between warehouse $w \in W$ and waste storage center $g \in G$.

EEH_{hg} : GHG emissions per unit of transported vaccine waste between healthcare center $h \in H$ and waste storage center $g \in G$.

EEG_{go} : GHG emissions per unit of transported vaccine waste between waste storage center $g \in G$ and waste treatment center $o \in O$.

EEO_{ol} : GHG emissions per unit of transported vaccine waste between waste treatment center $o \in O$ and landfills $l \in L$.

EOW_w : GHG emissions due to the construction of warehouse $w \in W$.

EOG_g : GHG emissions due to the construction of waste storage center $g \in G$.

EOO_o : GHG emissions due to the construction of treatment center $o \in O$.

EOL_l : GHG emissions due to the construction of landfill $l \in L$.

EIG_g : GHG emissions per unit of waste inventory in the waste storage center $g \in G$.

ETO_o : GHG emissions per unit of waste treated in the treatment center $o \in O$.

Social parameters

JS_{sw} : The number of jobs created due to the transported vaccine between supplier $s \in S$ and warehouse $w \in W$ per year.

JW_{wh} : The number of jobs created due to the transported vaccine units between warehouse $w \in W$ and healthcare center $h \in H$ per year.

JD_{wg} : The number of jobs created due to the transported defective vaccine units between warehouse $w \in W$ and waste storage center $g \in G$ per year.

JH_{hg} : The number of jobs created due to the transported vaccine waste units between healthcare center $h \in H$ and waste storage center $g \in G$ per year.

JG_{go} : The number of jobs created due to the transported vaccine waste units between waste storage center $g \in G$ and waste treatment center $o \in O$ per year.

JO_{ol} : The number of jobs created due to the transported vaccine waste units between waste treatment center $o \in O$ and landfills $l \in L$ per year.

JIG_g : The number of jobs created due to waste inventory in the waste storage center $g \in G$ per year.

JTO_o : The number of jobs created due to waste treated in the treatment center $o \in O$ per year.

Following the introduced notation, the deterministic model is formulated below.

Objective Function

The economic cost Z_1 is the same as in Chapter 3, which is to be minimized.

$$\text{Min } Z_1 = \text{Min } Z \quad (4.1)$$

$$\begin{aligned} \text{Min } Z_2 = & \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times EES_{sw} + \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QW_{whpt} \times \\ & (1 - \bar{p}) \times EEW_{wh} + \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} QD_{wgpt} \times \bar{p} \times EED_{wg} + \\ & \sum_{t \in T} \sum_{h \in H} \sum_{g \in G} QH_{hgt} \times EEH_{hg} + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times EEG_{go} + \\ & \sum_{t \in T} \sum_{o \in O} \sum_{l \in L} QO_{olt} \times EEO_{ol} + \sum_{t \in T} \sum_{w \in W} EOW_w \times \\ & \sum_{t \in T} \sum_{g \in G} EOG_g \times G_{gt} + \sum_{t \in T} \sum_{o \in O} EOO_o \times O_{ot} + \sum_{t \in T} \sum_{l \in L} EOL_l \times \\ & L_{lt} + \sum_{t \in T} \sum_{g \in G} INV_{gt} \times EIG_g + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times ETO_o \end{aligned} \quad (4.2)$$

$$\begin{aligned} \text{Max } Z_3 = & \sum_{t \in T} \sum_{s \in S} \sum_{w \in W} \sum_{p \in P} QS_{swpt} \times JS_{sw} + \sum_{t \in T} \sum_{w \in W} \sum_{h \in H} \sum_{p \in P} QW_{whpt} \times \\ & (1 - \bar{p}) \times JW_{wh} + \sum_{t \in T} \sum_{w \in W} \sum_{g \in G} \sum_{p \in P} QD_{wgpt} \times \bar{p} \times JD_{wg} + \sum_{t \in T} \sum_{h \in H} \sum_{g \in G} QH_{hgt} \times \\ & JH_{hg} + \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times JG_{go} + \sum_{t \in T} \sum_{o \in O} \sum_{l \in L} QO_{olt} \times JO_{ol} + \\ & \sum_{t \in T} \sum_{g \in G} \sum_{o \in O} QG_{got} \times JTO_o + \sum_{t \in T} \sum_{g \in G} INV_{gt} \times JIG_g \end{aligned} \quad (4.3)$$

Eq. (4.1), Eq. (4.2), and Eq. (4.3) minimize the total cost, environmental carbon emission and maximize job opportunities, respectively.

4.3 Solution Methodology

4.3.1 Robust optimization

The robust optimization approach is applied to address the uncertainties in the proposed framework, for more theoretical background and definitions see Chapter 3.

4.3.2 Weighted Goal Programming Approach

The presented problem is a multi-criteria optimization model with three objective functions. Therefore, a multi-objective optimization technique is needed to tackle the conflicting objectives and conduct meaningful analysis, we implement the weighted goal programming method due to its efficiency in dealing with multi-objectiveness. The standard formulation of weighted goal programming is given as follows.

$$\text{Min } Z_i = \sum_{i=1} w_i \left(\frac{d_i^+ + d_i^-}{g_i} \right) \quad (4.4)$$

$$\text{s.t } f_i(x) - d_i^+ + d_i^- = g_i \quad \forall i \in I \quad (4.5)$$

$$x \in X \quad (4.6)$$

$$d_i^+, d_i^- \geq 0 \quad \forall i \in I \quad (4.7)$$

Where

$i \in I$: represents the set of objective functions vector.

d_i^+, d_i^- : are deviational variables.

g_i : is the goal target for the i^{th} objective function.

$f_i(x)$: represents the i^{th} objective function.

w_i : reflects the weights for the i^{th} objective function based on priority, usually determined by the decision-makers.

The deterministic model is reformulated first based on robust optimization as in Chapter 3, and secondly following the weighted goal programming method to account for the three objective functions simultaneously. The weights w_1, w_2 and w_3 are set following the objective function priority, while goals, g_1, g_2 and g_3 are obtained by solving the problem with respect to each objective function independently. The reformulated model is presented as follows.

$$Min \beta = W_1\left(\frac{d_1^+}{g_1}\right) + W_2\left(\frac{d_2^+}{g_2}\right) + W_3\left(\frac{d_3^-}{g_3}\right) \quad (4.8)$$

Subject to:

Constraints 3.32 to 3.66

$$f_1(x) - d_1^+ + d_1^- = g_1 \quad (4.9)$$

$$f_2(x) - d_2^+ + d_2^- = g_2 \quad (4.10)$$

$$f_3(x) - d_3^+ + d_3^- = g_3 \quad (4.11)$$

$$d_i^+, d_i^- \geq 0 \quad \forall \quad i \in I \quad (4.12)$$

It can be observed from Eq. (4.8) that for both minimization objective functions in the economic and environmental costs, the positive deviational variables are introduced. While for maximizing social benefits the negative deviational variable is unwanted, therefore, it is penalized. Constraints (4.9) to (4.11) correspond respectively to Eq (4.1), Eq. (4.2), and Eq. (4.3) in the first problem, whereas Eq. (4.12) represents the non-negativity constraints of the deviational variables.

4.4 Results and Discussion

In this section, a realistic illustrative example that reflects real-world problems is investigated to validate the mathematical model applicability. It is worth mentioning that the input data are classified into (1) model parameters, (2) robust approach parameters, and (3) goal programming parameters. The goal programming and RO parameters are defined by the modeler or the decision-maker, while the majority of model parameters are assigned random values drawn from uniform distributions. Details of the illustrative example size and its corresponding input data are presented in the Appendix B.

The problem is coded in Python 3.11.4 and solved using Gurobi 10.0 on a Laptop Core (TM) i7 with 16 GB of RAM and a 3.00 GHz processor. the computational results obtained from the Gurobi solver are presented in Table 4.1 and Table 4.2 for both deterministic and robust models, respectively.

Objective functions (goals)	Values	Objective functions	Values	Deviational variables	Values
g_1	4.1572×10^7	$f_1(x)$	4.2606×10^7	d_1^+	1.0338×10^6
				d_1^-	0
g_2	1.8254×10^5	$f_2(x)$	1.8263×10^5	d_2^+	85.9392
				d_2^-	0
g_3	1.1387×10^5	$f_3(x)$	2.2593×10^4	d_3^+	9.1276×10^4
				d_3^-	0

Table 4.1: Deterministic model results.

Objective functions (goals)	Values	Objective functions	Values	Deviational variables	Values
g_1	6.8013×10^7	$f_1(x)$	6.8802×10^7	d_1^+	7.89360×10^5
				d_1^-	0
g_2	2.6584×10^5	$f_2(x)$	2.7454×10^5	d_2^+	8.693×10^3
				d_2^-	0
g_3	1.0809×10^5	$f_3(x)$	7.5110×10^4	d_3^+	9.1276×10^4
				d_3^-	0

Table 4.2: Results for the robust model with $\Gamma_i = |J_i|$

4.4.1 Effect of Uncertainty

First, we set the initial weights of the goal programming objective functions equal to $w_1 = 0.5$, $w_2 = 0.25$ and $w_3 = 0.25$ for the economic, environmental, and social aspects respectively. Following the initial weight assignments, the deterministic model is solved under the assumption of no uncertainty ($\Gamma_i = 0$) the obtained results are presented in Table 4.1. On the other hand, the robust model is also solved under the same weights assumption with a set size of $\Gamma_i = |J_i|$ in the worst case scenario, Table 4.2 shows the finding results. It can be observed that the analysis reveals a deterioration in the objective function values under the robust model compared to the deterministic model, highlighting the negative consequences of uncertainty on the problem at hand. The obtained results offer decision-makers actionable guidance on determining the optimal level of robustness to hedge against potential parameter vari-

ations. This strategic investment, known as the "price of robustness," can improve the network performance and responsiveness, leading to high demand fulfillment, reduced shortages, waste management, and a more resilient vaccine supply chain network.

4.4.2 Weight Sensitivity Analysis

The proposed multi-objective problem requires weight assignments for each objective which are usually obtained by industry professionals or decision-makers. In this work, expert judgment is not utilized which motivates us to set an initial starting assumption with equal weights. These combinations of weight might not cover all the solution space of weights that the decision-maker could make use of. Moreover, exploring all possible solutions could be time-consuming due to the large possible combinations and might result in impractical solutions for policymakers. Building upon Jones's methodology [49], the objective function incorporates weightings for each criterion to prevent overly extreme or uneven solutions and assess the performance of the proposed model. This approach yields 10 solutions that encompass the three key criteria of economic, environmental, and social aspects, as presented in Table 4.3. We set the initial weight combination equals at first, then tune it to see its effect on the three objective functions. The obtained results are depicted in Table 4.4 and Figure 4.1, it can be observed that the three objectives are sensitive to weight variation. For instance, the economic cost provides its lowest value at a weight of 0.6, similarly, the environmental objective and social aspects achieve their preferable lowest and highest values respectively at the same value of weight. On the other hand, the economic and environmental cost reach their worst values (highest cost) at scenario

Combinations	Weights		
	$w_1(\text{economic})$	$w_2(\text{Environmental})$	$w_3(\text{Social})$
S_1	0.333	0.333	0.333
S_2	0.5	0.25	0.25
S_3	0.25	0.5	0.25
S_4	0.25	0.25	0.5
S_5	0.6	0.2	0.2
S_6	0.2	0.6	0.2
S_7	0.2	0.2	0.6
S_8	0.42	0.29	0.29
S_9	0.29	0.42	0.29
S_{10}	0.29	0.29	0.42

Table 4.3: Weights combinations.

three with a weight of 0.25 and scenario eight with a weight of 0.2 respectively, while the social aspects take their lowest value at scenario six with a weight of 0.2, we can also notice a trade-off of the social objective with respect to the economic and environmental costs. Overall, a compromised combination of these weights should be set based on the decision-maker preferences to obtain the desired solution, for instance, scenario S_5 serves as a standard reference of weight combination for risk-averse decision makers. However, for an environmentalist policymaker, scenario S_6 could be a potential combination. If the decision-maker seeking more sustainable job opportunities then a combination S_7 would be a better choice, while incurring greater economic and environmental burdens.

4.4.3 Sensitivity Analysis

To see the effect of parameter deviation on the three objective functions, a sensitivity analysis is conducted on the following parameters with a set size of $\Gamma_i = |J_i|$:

- Demand uncertainty ($\tilde{D}_{hpt}$).

Scenarios	w_1	w_2	w_3	β	$f_1(x)$	$f_2(x)$	$f_3(x)$
S_1	0.33	0.33	0.33	2.460×10^{-1}	6.8880×10^7	2.7403×10^5	3.2923×10^4
S_2	0.5	0.25	0.25	1.876×10^{-1}	6.8802×10^7	2.7454×10^5	3.2980×10^4
S_3	0.25	0.5	0.25	1.887×10^{-1}	7.0488×10^7	2.7107×10^5	3.2603×10^4
S_4	0.25	0.25	0.5	3.608×10^{-1}	6.9519×10^7	2.7878×10^5	3.3451×10^4
S_5	0.6	0.2	0.2	1.441×10^{-1}	6.8503×10^7	2.7702×10^5	3.3255×10^4
S_6	0.2	0.6	0.2	1.576×10^{-1}	7.0453×10^7	2.7058×10^5	3.2552×10^4
S_7	0.2	0.2	0.6	4.311×10^{-1}	7.0461×10^7	2.8376×10^5	3.4147×10^4
S_8	0.42	0.29	0.29	2.090×10^{-1}	6.8724×10^7	2.7657×10^5	3.3201×10^4
S_9	0.29	0.42	0.29	2.148×10^{-1}	6.9811×10^7	2.7206×10^5	3.2707×10^4
S_{10}	0.29	0.29	0.42	3.083×10^{-1}	6.9286×10^7	2.7690×10^5	3.3236×10^4

Table 4.4: Sensitivity analysis to weights variations with $\Gamma_i = |J_i|$.

- Inspection errors $(\tilde{\gamma}_1, \tilde{\gamma}_2)$.
- Vaccine waste uncertainty $(\widetilde{VW}_{ht})$.
- Defective treatment rate $(\tilde{\theta})$.

To perform the analysis, a variation of parameters in the interval of +5 %, +10 %, +15 %, +20 %, and +25 % of deviations from the nominal values are taken into consideration, while scenario S_2 of weights combination from the previous weight analysis in Table 4.4 is utilized as a reference to conduct this sensitivity. The finding results are shown in Table A.1, while a significant representation of the obtained results is depicted in Figure 4.2.

Figure 4.2 illustrates the behavior of the three objective functions against different percentages of uncertain parameter variation. It is worth mentioning that some objective functions are less sensitive to parameter fluctuations. From Figure 4.2 (a) and for 5 % and 10 % of demand perturbation we can observe a sharp increase in the economic cost f_1 with almost 59 % of deviation from its deterministic counterpart, this behavior can be justified by the direct effect and sensitivity of the total cost to

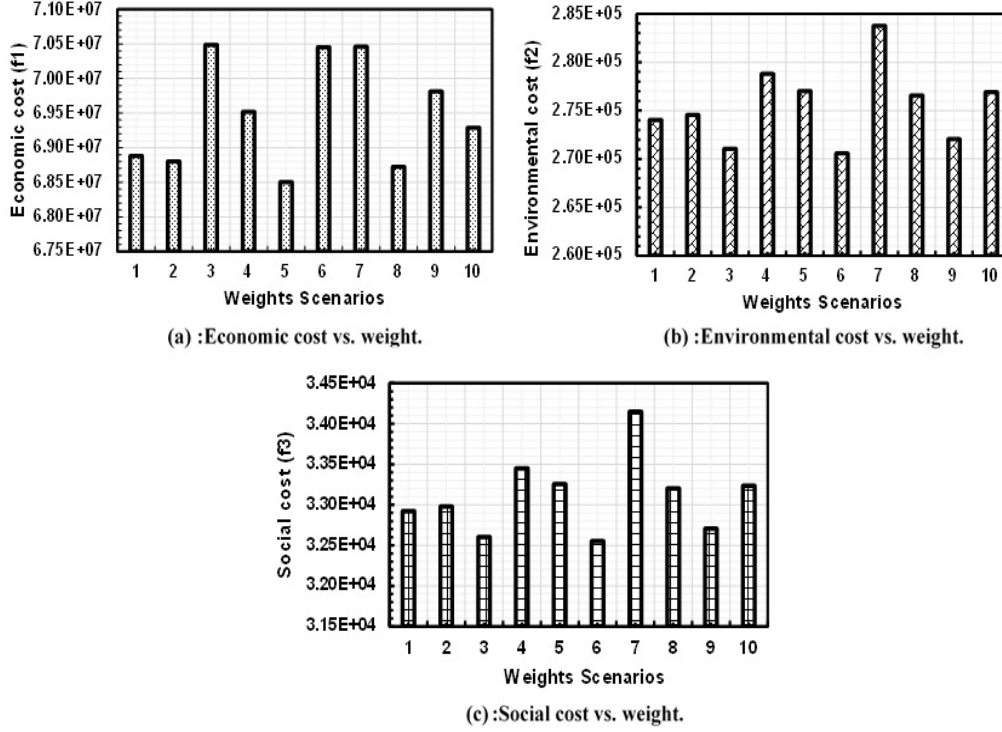


Figure 4.1: Objective functions vs. weights.

demand variation. Nonetheless, the same demand variations result in a 45 % and 47 % deterioration (increase) in the environmental cost f_2 , and up to 2.6 % and 1.8% increase in the social aspects. When it comes to parameter deviation of vaccine waste in Figure 4.2 (b), with 15 % and 20 % of changes in vaccine waste a significant surge in the total cost is noticed of almost 61 % and 62 % of increase from its nominal value. Correspondingly, with the same perturbation, the environmental cost achieves 50 %, and 52 % of the surge is obtained. While the social cost is almost unchanged in the context. The same analysis is applicable to inspection error deviation in Figure 4.2 (c) where the economic cost is more pronounced against parameter fluctuation compared to the environmental and social aspects. In the context of Figure 4.2 (d) it can be seen that almost all three objectives are fluctuating in values with respect to

treatment rate parameter perturbation, this could be reflected by the fact that these objectives are less sensitive to the changes in this parameter.

In general, the results demonstrate that among all objectives in the network, economic cost experiences the most significant impact from parameter variations. Focusing on demand uncertainty introduced in the first step, our analysis reveals a significant increase in total cost, with a more pronounced impact observed at a 25 % deviation from the nominal value. Similar to the previously observed impact of demand uncertainty, an analysis of inspection error uncertainties reveals a considerable cost increase primarily attributable to the production of defective vaccines, which directly disrupts supply chains and contributes to increased shortages at healthcare centers. Moreover, an important finding is that uncertainties in both vaccine waste and treatment rate significantly impact total cost deterioration. This is further exacerbated by the strategic decision to open additional facilities in response to such parameter variations, leading to a substantial cost increase.

4.5 Theoretical and Practical Implications

This study emphasized the significance of incorporating defective vaccine item considerations and sustainable multi-objective vaccine supply chain aspects within the network under uncertainty. The research highlighted the primary gain of incorporating these uncertainties as it enhances both strategic and tactical planning and activities across the supply chain. Furthermore, the findings demonstrate that incorporating demand and inspection errors uncertainties facilitates timely responses to

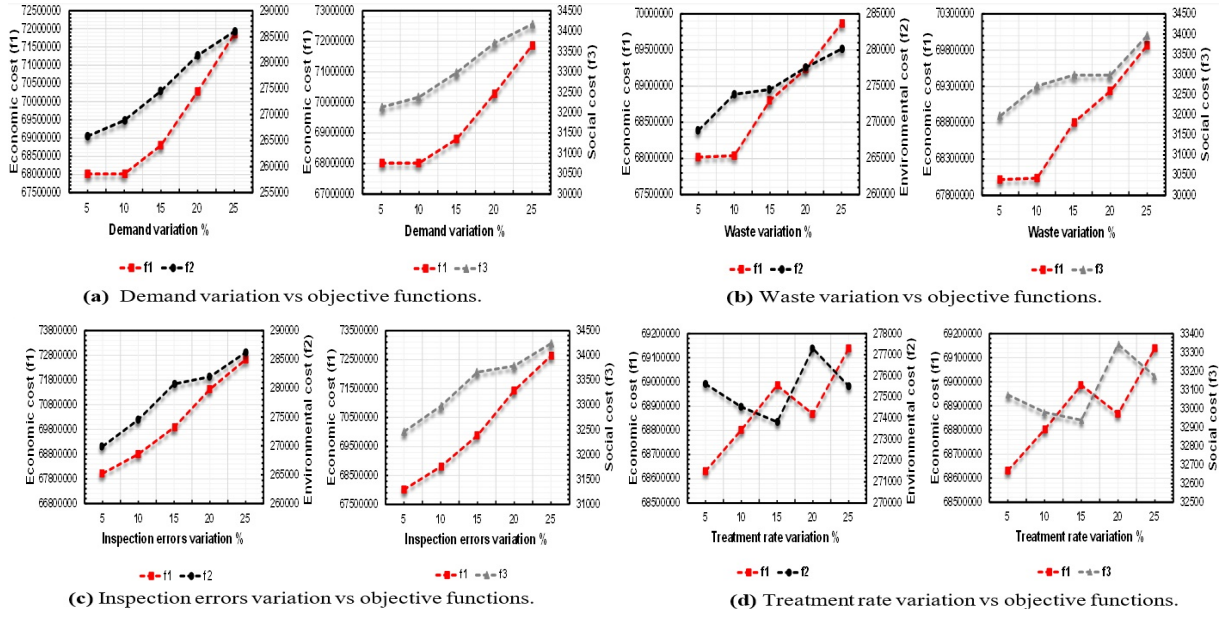


Figure 4.2: Sensitivity analysis of the uncertain parameter.

any unforeseen shortages and thus fulfills the needs of healthcare centers and strengthens the robustness of the network against any future parameter fluctuation, thereby mitigating any disruption and providing rapid access to vaccine items in a short time. Furthermore, this research expands the scope by incorporating sustainability considerations through the inclusion of uncertainties not only in supply-demand but also in vaccine waste generated by healthcare facilities during massive vaccination campaigns. This comprehensive approach aims to equip healthcare decision-makers with strategic and tactical insights to proactively hedge against potential parameter fluctuations and develop robust solutions, particularly in the context of outbreaks like COVID-19. Finally, considering defective vaccine supply chain under multiple uncertainties and objectiveness could be a cumbersome to decision-makers, thus by introducing this work for the first time we empower managers to efficiently manage real-world uncertainties and ensure timely responsiveness while minimizing shortages. This is achieved

through determining the optimal quantities and resources required among echelons and designing a better planning for healthcare policy-makers.

4.6 Conclusion

The recent disruptions of the vaccine supply chain due to various factors highlight the urgent need for faster and equitable vaccine access. Surging demand, coupled with massive waste from vaccination campaigns, makes it further complicated. Moreover, the drastic effect of supply chain systems on the carbon footprint emissions along with job crises that appeared recently due to the controlling measures of the COVID-19 pandemic make it worse. This calls for designing a more sustainable vaccine supply chain network taking into consideration these issues. In this work, we design a sustainable vaccine supply chain under imperfect items and uncertainty taking into account economic, environmental, and social aspects simultaneously. The goal programming approach is used to deal with multi-objectiveness while a combined polyhedral-interval robust optimization approach is followed to handle different uncertainties and hedge against future parameter fluctuation not only for demand uncertainty but also for inspection errors, vaccine waste, and defective treatment rate. The result obtained from the illustrative example shows that the proposed method achieves robustness by increasing the optimal values to its worst-case scenario as the price of robustness. The sensitivity analysis also shows : (1) the proposed supply chain network is more sensitive to parameter deviation, as the level of uncertainty increases the optimal cost deteriorates, (2) demand variation along with inspection errors have

the greatest impact on the multi-objective vaccine supply chain network (3) the treatment rate uncertainty has its least effect on the three objectives, (4) while a better choice of weights for an optimal cost function is left to decision-makers preferences.

CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

In this chapter, we summarize the thesis contributions and outline potential future research avenues.

5.1 Work Summary

This thesis has considered a novel framework arising from supply chain management which was solved in two different ways: a single and a multi-objective objective vaccine supply chain under uncertainty and defects. For the single objective model, we consider the four uncertain parameters : (1) demand, (2) inspection errors, (3) vaccine waste, and (4) defective treatment rate for the first time. To account for these uncertainties the RO approach is adopted, while a LRA is introduced to solve large-scale instances. Additionally, to address the decision-maker's risk tolerance a priori bound on constraint violation approach is employed. Overall, the proposed framework has

been solved successfully and can generate less conservative solutions compared to its rivals.

For the multi-objective problem, the same uncertainties have been considered and dealt with by a robust optimization approach. While multi-objectiveness has been solved by a goal programming method. Finally, the model performance has been tested through a sensitivity analysis.

5.2 Future Research

Future research can be conducted in the following aspects.

Methodologically speaking, the uncertainties such as demand could be captured using federated machine learning technique. Further research could also involve expanding the proposed model to incorporate inventory in healthcare centers along with perishability and cold chain. Incorporating dynamic vaccine centers that are easy to relocate to satisfy demand along with routing could be another interesting extension.

APPENDIX A

SENSITIVITY ANALYSIS :

TABLE A.1

Variables	Values of $\widetilde{D}_{hpt}$				
	5 %	10 %	15 %	20 %	20 %
$f_1(x)$	6.8013×10^7	6.8013×10^7	6.8802×10^7	7.0279×10^7	7.1857×10^7
$f_2(x)$	2.6585×10^5	2.6888×10^5	2.7454×10^5	2.8138×10^5	2.8598×10^5
$f_3(x)$	3.2131×10^4	3.2379×10^4	3.2980×10^4	3.3703×10^4	3.4167×10^4
β	1.7568×10^{-1}	1.7796×10^{-1}	1.8769×10^{-1}	2.0331×10^{-1}	2.1816×10^{-1}
Variables	Values of $\widetilde{VW}_{ht}$				
	5%	10%	15%	20%	25%
$f_1(x)$	6.8017×10^7	6.8038×10^7	6.8802×10^7	6.9238×10^7	6.9866×10^7
$f_2(x)$	2.6889×10^5	2.7386×10^5	2.7454×10^5	2.7758×10^5	2.8014×10^5
$f_3(x)$	3.1971×10^4	3.2712×10^4	3.2980×10^4	3.3502×10^4	3.3963×10^4
β	1.8205×10^{-1}	1.7796×10^{-1}	1.8769×10^{-1}	1.9254×10^{-1}	1.9850×10^{-1}
Variables	Values of $\widetilde{VW}_{ht}$				
	5%	10%	15%	20%	25%
$f_1(x)$	6.8017×10^7	6.8038×10^7	6.8802×10^7	6.9238×10^7	6.9866×10^7
$f_2(x)$	2.6889×10^5	2.7386×10^5	2.7454×10^5	2.7758×10^5	2.8014×10^5
$f_3(x)$	3.1971×10^4	3.2712×10^4	3.2980×10^4	3.3502×10^4	3.3963×10^4
β	1.8205×10^{-1}	1.7796×10^{-1}	1.8769×10^{-1}	1.9254×10^{-1}	1.9850×10^{-1}
Variables	Values of $\widetilde{\gamma}_1, \widetilde{\gamma}_2$				
	5%	10%	15%	20%	25%
$f_1(x)$	6.8013×10^7	6.8013×10^7	6.8013×10^7	7.1428×10^7	7.2629×10^7
$f_2(x)$	2.6990×10^5	2.7454×10^5	2.8074×10^5	2.8200×10^5	2.8622×10^5
$f_3(x)$	3.2463×10^4	3.2980×10^4	3.3664×10^4	3.3789×10^4	3.4240×10^4
β	1.7873×10^{-1}	1.7873×10^{-1}	1.9989×10^{-1}	2.1215×10^{-1}	2.2389×10^{-1}
Variables	Values of $\widetilde{\theta}$				
	5%	10%	15%	20%	25%
$f_1(x)$	6.8631×10^7	6.8802×10^7	6.8986×10^7	6.8867×10^7	6.9139×10^7
$f_2(x)$	2.7562×10^5	2.7454×10^5	2.7383×10^5	2.7729×10^5	2.7729×10^5
$f_3(x)$	3.3073×10^4	3.2980×10^4	3.2938×10^4	3.3343×10^4	3.3172×10^4
β	1.8724×10^{-1}	1.8065×10^{-1}	1.8847×10^{-1}	1.8992×10^{-1}	1.9063×10^{-1}

Table A.1: Sensitivity analysis to parameters variation with $\Gamma_i = |J_i|$.

APPENDIX B

SIZE OF PROBLEM 1 & 2 AND DATA INPUT

Problem scale	Instances	L	O	G	H	W	S	T	P
Small	I_1	3	3	3	3	3	3	12	3
Medium	I_2	4	3	4	6	5	3	12	3
	I_3	4	3	4	8	5	3	14	3
Large	I_4	4	3	4	14	5	3	12	3
	I_5	5	3	5	20	5	4	16	3
	I_6	5	3	5	25	5	4	16	3

Table B.1: Size of problem 1.3.

	T	P	S	W	H	G	O	L
Size of the problem	12	3	4	4	6	4	4	4

Table B.2: Size problem 2.4.

Parameters	Values	Parameters	Values
FS_s	Uniform (15000, 25000)	p	Uniform (0.05,0.1)
FW_w	Uniform (14000, 30000)	(1-p)	Uniform (0.9,0.95)
FG_g	Uniform (12000, 20000)	γ_1	Uniform (0.05,0.1)
FO_o	Uniform (2000, 5000)	γ_2	Uniform (0.05,0.1)
FL_l	Uniform (500,2000)	TS_{sw}	Uniform (100,500)
D_{hpt}	Uniform (20,500)	TW_{wh}	Uniform (100,400)
VW_{ht}	Uniform (10,200)	TG_{wg}	Uniform (90,350)
KW_{wp}	Uniform (10,100)	TH_{hg}	Uniform (40,250)
HCW_{wp}	Uniform (20,150)	TM_{go}	Uniform (150,300)
p_{hp}	Uniform (80,200)	TO_{ol}	Uniform (100,900)
c_{sp}	Uniform (20,100)	CS_{sp}	Uniform (4000, 80000)
HCG_g	Uniform (80,170)	CW_{wp}	Uniform (1000,4000)
TC_o	Uniform (100,300)	CG_g	Uniform (1000,3000)
θ	Uniform (0.05,0.2)	CO_o	Uniform (45000,60000)
I_{wp}	Uniform (50,200)	CL_l	Uniform (3000, 50000)

Table B.3: Input data

REFERENCES

- [1] D. D. Wu and D. L. Olson, *Pandemic Risk Management in Operations and Finance: Modeling the Impact of COVID-19*, ser. Computational Risk Management. Cham: Springer International Publishing, 2020. [Online]. Available: <https://link.springer.com/10.1007/978-3-030-52197-4>
- [2] D. Ivanov, “Predicting the impacts of epidemic outbreaks on global supply chains: A simulation-based analysis on the coronavirus outbreak (COVID-19/SARS-CoV-2) case,” *Transportation Research Part E: Logistics and Transportation Review*, vol. 136, p. 101922, Apr. 2020. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S1366554520304300>
- [3] Y. Yang, H. Bidkhori, and J. Rajgopal, “Optimizing vaccine distribution networks in low and middle-income countries,” *Omega*, vol. 99, p. 102197, Mar. 2021. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0305048319307236>
- [4] L. E. Duijzer, W. van Jaarsveld, and R. Dekker, “Literature review: The vaccine supply chain,” *European Journal of Operational Research*, vol.

- 268, no. 1, pp. 174–192, Jul. 2018, number: 1. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0377221718300158>
- [5] L. Tang, Y. Li, D. Bai, T. Liu, and L. C. Coelho, “Bi-objective optimization for a multi-period COVID-19 vaccination planning problem,” *Omega*, vol. 110, p. 102617, Jul. 2022. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0305048322000263>
- [6] T. K. Dasaklis, C. P. Pappis, and N. P. Rachaniotis, “Epidemics control and logistics operations: A review,” *International Journal of Production Economics*, vol. 139, no. 2, pp. 393–410, Oct. 2012, number: 2. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0925527312002150>
- [7] W. H. Chooi, P. W. Ng, Z. Hussain, L. C. Ming, B. Ibrahim, and D. Koh, “Vaccine contamination: Causes and control,” *Vaccine*, vol. 40, no. 12, pp. 1699–1701, Mar. 2022, number: 12. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0264410X22001694>
- [8] G. Blair, “Japan’s Moderna Covid vaccine rollout hit by recall and contamination scares,” *The Guardian*, Sep. 2021. [Online]. Available: <https://www.theguardian.com/world/2021/sep/02/japans-moderna-covid-vaccine-rollout-hit-by-recall-and-contamination-scares>
- [9] “The World Economic Forum,” Feb. 2023. [Online]. Available: <https://www.weforum.org/>

- [10] C. Le Quéré, R. B. Jackson, M. W. Jones, A. J. P. Smith, S. Abernethy, R. M. Andrew, A. J. De-Gol, D. R. Willis, Y. Shan, J. G. Canadell, P. Friedlingstein, F. Creutzig, and G. P. Peters, “Temporary reduction in daily global CO₂ emissions during the COVID-19 forced confinement,” *Nature Climate Change*, vol. 10, no. 7, pp. 647–653, Jul. 2020, number: 7 Publisher: Nature Publishing Group. [Online]. Available: <https://www.nature.com/articles/s41558-020-0797-x>
- [11] “The impact of COVID-19 on employment and jobs - OECD,” Feb. 2023. [Online]. Available: <https://www.oecd.org/employment/covid-19.htm>
- [12] H. Gilani and H. Sahebi, “A data-driven robust optimization model by cutting hyperplanes on vaccine access uncertainty in COVID-19 vaccine supply chain,” *Omega*, vol. 110, p. 102637, Jul. 2022. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0305048322000457>
- [13] V. K. Manupati, T. Schoenherr, N. Subramanian, M. Ramkumar, B. Soni, and S. Panigrahi, “A multi-echelon dynamic cold chain for managing vaccine distribution,” *Transportation Research Part E: Logistics and Transportation Review*, vol. 156, p. 102542, Dec. 2021. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S136655452100301X>
- [14] D. Bertsimas, V. Digalakis Jr, A. Jacquillat, M. L. Li, and A. Previero, “Where to locate COVID-19 mass vaccination facilities?” *Naval Research Logistics (NRL)*, vol. 69, no. 2, pp. 179–200, 2022, number: 2 _eprint:

- <https://onlinelibrary.wiley.com/doi/pdf/10.1002/nav.22007>. [Online]. Available: <https://onlinelibrary.wiley.com/doi/abs/10.1002/nav.22007>
- [15] M. Rastegar, M. Tavana, A. Meraj, and H. Mina, “An inventory-location optimization model for equitable influenza vaccine distribution in developing countries during the COVID-19 pandemic,” *Vaccine*, vol. 39, no. 3, pp. 495–504, Jan. 2021, number: 3.
- [16] S. Shukla, F. Fressin, M. Un, H. Coetzer, and S. K. Chaguturu, “Optimizing vaccine distribution via mobile clinics: a case study on COVID-19 vaccine distribution to long-term care facilities,” *Vaccine*, vol. 40, no. 5, pp. 734–741, Jan. 2022, number: 5. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0264410X21016571>
- [17] M. Shiri and F. Ahmadizar, “An equitable and accessible vaccine supply chain network in the epidemic outbreak of COVID-19 under uncertainty,” *Journal of Ambient Intelligence and Humanized Computing*, Jun. 2022. [Online]. Available: <https://doi.org/10.1007/s12652-022-03865-2>
- [18] K. De Boeck, C. Decouttere, and N. Vandaele, “Vaccine distribution chains in low- and middle-income countries: A literature review,” *Omega*, vol. 97, p. 102097, Dec. 2020. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0305048319304098>
- [19] H. Jahani, A. E. Chaleshtori, S. M. S. Khaksar, A. Aghaie, and J.-B. Sheu, “COVID-19 vaccine distribution planning using a congested queuing

- system—A real case from Australia,” *Transportation Research Part E: Logistics and Transportation Review*, vol. 163, p. 102749, Jul. 2022. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S1366554522001405>
- [20] L. A. Haidari, B. Wahl, S. T. Brown, L. Privor-Dumm, C. Wallman-Stokes, K. Gorham, D. L. Connor, A. R. Wateska, B. Schreiber, H. Dicko, P. Jaillard, M. Avella, and B. Y. Lee, “One size does not fit all: The impact of primary vaccine container size on vaccine distribution and delivery,” *Vaccine*, vol. 33, no. 28, pp. 3242–3247, Jun. 2015, number: 28.
- [21] X. Luo and W. Liao, “Collaborative reverse logistics network for infectious medical waste management during the covid-19 outbreak,” *International Journal of Environmental Research and Public Health*, vol. 19, no. 15, p. 9735, 2022.
- [22] H. Yu, X. Sun, W. D. Solvang, and X. Zhao, “Reverse Logistics Network Design for Effective Management of Medical Waste in Epidemic Outbreaks: Insights from the Coronavirus Disease 2019 (COVID-19) Outbreak in Wuhan (China),” *International Journal of Environmental Research and Public Health*, vol. 17, no. 5, p. 1770, Jan. 2020, number: 5 Publisher: Multidisciplinary Digital Publishing Institute. [Online]. Available: <https://www.mdpi.com/1660-4601/17/5/1770>
- [23] S. Kargar, M. Pourmehdi, and M. M. Paydar, “Reverse logistics network design for medical waste management in the epidemic outbreak of the novel coronavirus (COVID-19),” *Science of The Total Environment*, vol. 746, p. 141183, Dec. 2020. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0048969720347124>

- [24] C. Cao, Y. Xie, Y. Liu, J. Liu, and F. Zhang, “Two-phase COVID-19 medical waste transport optimisation considering sustainability and infection probability,” *Journal of Cleaner Production*, vol. 389, p. 135985, Feb. 2023. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0959652623001439>
- [25] J. L. Higle, “Stochastic Programming: Optimization When Uncertainty Matters,” in *Emerging Theory, Methods, and Applications*, ser. INFORMS TutORials in Operations Research. INFORMS, Sep. 2005, pp. 30–53, section: 2. [Online]. Available: <https://pubsonline.informs.org/doi/abs/10.1287/educ.1053.0016>
- [26] A. Ben-Tal, D. den Hertog, and J.-P. Vial, “Deriving robust counterparts of nonlinear uncertain inequalities,” *Mathematical Programming*, vol. 149, no. 1, pp. 265–299, Feb. 2015. [Online]. Available: <https://doi.org/10.1007/s10107-014-0750-8>
- [27] A. L. Soyster, “Technical Note—Convex Programming with Set-Inclusive Constraints and Applications to Inexact Linear Programming,” *Operations Research*, vol. 21, no. 5, pp. 1154–1157, Oct. 1973, publisher: INFORMS. [Online]. Available: <https://pubsonline.informs.org/doi/abs/10.1287/opre.21.5.1154>
- [28] A. Ben-Tal, B. Golany, A. Nemirovski, and J.-P. Vial, “Retailer-Supplier Flexible Commitments Contracts: A Robust Optimization Approach,” *Manufacturing & Service Operations Management*, vol. 7, no. 3, pp. 248–271, Jul. 2005, number: 3. [Online]. Available: <http://pubsonline.informs.org/doi/10.1287/msom.1050.0081>

- [29] D. Bertsimas and M. Sim, “The Price of Robustness,” *Operations Research*, vol. 52, no. 1, pp. 35–53, Feb. 2004, publisher: INFORMS. [Online]. Available: <https://pubsonline.informs.org/doi/10.1287/opre.1030.0065>
- [30] E. Ensar Işık and S. Topaloglu Yildiz, “Optimizing the COVID-19 cold chain vaccine distribution network with medical waste management: A robust optimization approach,” *Expert Systems with Applications*, vol. 229, p. 120510, Nov. 2023. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0957417423010126>
- [31] F. Habibi, A. Abbasi, and R. K. Chakraborty, “Designing an efficient vaccine supply chain network using a two-phase optimization approach: a case study of COVID-19 vaccine,” *International Journal of Systems Science: Operations & Logistics*, vol. 10, no. 1, p. 2121623, Dec. 2023, publisher: Taylor & Francis _eprint: <https://doi.org/10.1080/23302674.2022.2121623>. [Online]. Available: <https://doi.org/10.1080/23302674.2022.2121623>
- [32] Z. Sazvar, K. Tafakkori, N. Oladzad, and S. Nayeri, “A capacity planning approach for sustainable-resilient supply chain network design under uncertainty: A case study of vaccine supply chain,” *Computers & Industrial Engineering*, vol. 159, p. 107406, Sep. 2021. [Online]. Available: <https://linkinghub.elsevier.com/retrieve/pii/S0360835221003107>
- [33] S. E. Chick, H. Mamani, and D. Simchi-Levi, “Supply Chain Coordination and Influenza Vaccination,” *Operations Research*, vol. 56, no. 6, pp. 1493–1506,

- Dec. 2008, number: 6. [Online]. Available: <http://pubsonline.informs.org/doi/10.1287/opre.1080.0527>
- [34] B. Y. Lee, T.-M. Assi, K. Rookkapan, A. R. Wateska, J. Rajgopal, V. Sornsrivichai, S.-I. Chen, S. T. Brown, J. Welling, B. A. Norman, D. L. Connor, R. R. Bailey, A. Jana, W. G. Van Panhuis, and D. S. Burke, "Maintaining Vaccine Delivery Following the Introduction of the Rotavirus and Pneumococcal Vaccines in Thailand," *PLoS ONE*, vol. 6, no. 9, p. e24673, Sep. 2011, number: 9. [Online]. Available: <https://dx.plos.org/10.1371/journal.pone.0024673>
- [35] S. Abbasi, S. Zahmatkesh, A. Bokhari, and M. Hajiaghahi-Keshteli, "Designing a vaccine supply chain network considering environmental aspects," *Journal of Cleaner Production*, vol. 417, p. 137935, Sep. 2023. [Online]. Available: <https://linkinghub.elsevier.com/retrieve/pii/S0959652623020930>
- [36] C. Li, J.-Y. Dai, and X. Li, "Imperfect Vaccination Evolutionary Game Incorporating Individual Social Difference and Subjective Perception," *IEEE Transactions on Computational Social Systems*, pp. 1–14, 2023. [Online]. Available: <https://ieeexplore.ieee.org/document/10124338/>
- [37] M. A. Kamran, R. Kia, F. Goodarzian, and P. Ghasemi, "A new vaccine supply chain network under COVID-19 conditions considering system dynamic: Artificial intelligence algorithms," *Socio-Economic Planning Sciences*, vol. 85, p. 101378, Feb. 2023. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0038012122001732>

- [38] H. F. Rahman, R. K. Chakraborty, S. K. Paul, and S. Elsayah, “Optimising vaccines supply chains to mitigate the COVID-19 pandemic,” *International Journal of Systems Science: Operations & Logistics*, vol. 10, no. 1, p. 2122757, Dec. 2023, publisher: Taylor & Francis _eprint: <https://doi.org/10.1080/23302674.2022.2122757>. [Online]. Available: <https://doi.org/10.1080/23302674.2022.2122757>
- [39] B. L. Gorissen, . Yanıkoğlu, and D. den Hertog, “A practical guide to robust optimization,” *Omega*, vol. 53, pp. 124–137, Jun. 2015. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0305048314001698>
- [40] Z. Li, R. Ding, and C. A. Floudas, “A Comparative Theoretical and Computational Study on Robust Counterpart Optimization: I. Robust Linear Optimization and Robust Mixed Integer Linear Optimization,” *Industrial & Engineering Chemistry Research*, vol. 50, no. 18, pp. 10 567–10 603, Sep. 2011, number: 18. [Online]. Available: <https://pubs.acs.org/doi/10.1021/ie200150p>
- [41] S. H. Alavi and A. Jabbarzadeh, “Supply chain network design using trade credit and bank credit: A robust optimization model with real world application,” *Computers & Industrial Engineering*, vol. 125, pp. 69–86, Nov. 2018. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0360835218303772>
- [42] B. Hamdan and A. Diabat, “Robust design of blood supply chains under risk of disruptions using Lagrangian relaxation,” *Transportation Research*

- Part E: Logistics and Transportation Review*, vol. 134, p. 101764, Feb. 2020. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S1366554518300656>
- [43] A. Yousefi-Babadi, A. Bozorgi-Amiri, R. Tavakkoli-Moghaddam, and K. Govindan, “Redesign of the sustainable wheat-flour-bread supply chain network under uncertainty: An improved robust optimization,” *Transportation Research Part E: Logistics and Transportation Review*, vol. 176, p. 103215, Aug. 2023. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S136655452300203X>
- [44] M. L. Fisher, “The Lagrangian Relaxation Method for Solving Integer Programming Problems,” *Management Science*, vol. 50, no. 12_supplement, pp. 1861–1871, Dec. 2004, publisher: INFORMS. [Online]. Available: <https://pubsonline.informs.org/doi/abs/10.1287/mnsc.1040.0263>
- [45] Z. Li, Q. Tang, and C. A. Floudas, “A Comparative Theoretical and Computational Study on Robust Counterpart Optimization: II. Probabilistic Guarantees on Constraint Satisfaction,” *Industrial & Engineering Chemistry Research*, vol. 51, no. 19, pp. 6769–6788, May 2012, number: 19 Publisher: American Chemical Society. [Online]. Available: <https://doi.org/10.1021/ie201651s>
- [46] I. Paschalidis and Seong-Cheol Kang, “Robust Linear Optimization: On the benefits of distributional information and applications in inventory control,” in *Proceedings of the 44th IEEE Conference on Decision and*

- Control*. Seville, Spain: IEEE, 2005, pp. 4416–4421. [Online]. Available: <http://ieeexplore.ieee.org/document/1582857/>
- [47] Y. A. Guzman, L. R. Matthews, and C. A. Floudas, “New a priori and a posteriori probabilistic bounds for robust counterpart optimization: I. Unknown probability distributions,” *Computers & Chemical Engineering*, vol. 84, pp. 568–598, Jan. 2016. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0098135415003099>
- [48] —, “New a priori and a posteriori probabilistic bounds for robust counterpart optimization: II. A priori bounds for known symmetric and asymmetric probability distributions,” *Computers & Chemical Engineering*, vol. 101, pp. 279–311, Jun. 2017. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0098135416302228>
- [49] D. Jones, “A practical weight sensitivity algorithm for goal and multiple objective programming,” *European Journal of Operational Research*, vol. 213, no. 1, pp. 238–245, Aug. 2011. [Online]. Available: <https://www.sciencedirect.com/science/article/pii/S0377221711002232>

VITAE

- Name: Abderrahmen Bouchenine
- Email: *a23.rrahman@gmail.com*
- Address: King Fahd University of Petroleum and Minerals.

Publications & achievements

- **Bouchenine, A., & Almaraj, I.** (2023). A robust optimization approach model for a multi-vaccine multi-echelon supply chain, 50th *international conference in Computers and Industrial Engineering* , Sharjah UAE.
- **Bouchenine, A., & Almaraj, I.** A robust optimization design of vaccine supply chain with defects and waste under multiple uncertainties. submitted to *Production and Operations Management, POMS*.
- **Bouchenine, A., & Almaraj, I.** A multi-objective robust optimization model with defective vaccine and reverse supply chain under uncertainty. **In preparation.**