ALLOCATING VACCINES UNDER SCARCE SUPPLY

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By
Onur Kılınç
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We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

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ABSTRACT

ALLOCATING VACCINES UNDER SCARCE SUPPLY

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We consider the vaccine allocation problem under scarce supply. We formulate the problem as a two stage stochastic programming model, considering the uncertain factors such as vaccine efficacy, disease spread dynamics and the amount of future supply. We discuss two variants of the model that could be used under different preferences. We demonstrate the usability of our formulations on two case study examples that are generated based on real-life data. The results demonstrate that incorporating the uncertainty in these factors into the decision making process would allow the policy makers to use more effective strategies with an adaptive nature. This is also indicated by the value of stochastic solution, which shows a significant enhancement in disease control gained by the stochastic programming solution compared to a plan based on expected figures.

Keywords: Vaccine allocation, Stochastic Programming.

ÖZET

SINIRLI TEDARIK DURUMUNDA AŞI DAĞITIMI

Onur Kılınç
Endüstri Mühendisliği, Yüksek Lisans
Tez Danışmanı: Özlem Karsu
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Bu çalışmada, sınırlı arz koşulları altındaki aşı dağıtımı problemi ele alınmıştır. Aşı etkililiği, hastalık yayılma dinamikleri ve gelecekteki arz miktarı gibi belirsiz faktörleri dikkate alan iki aşamalı stokastik program modeli olarak bu problem formüle edilmiştir. Farklı tercihler altında kullanılabilecek iki model varyasyonu incelenmiş ve sonuçları karşılaştırılmıştır. Formülasyonlarımızın kullanılabilirliği, gerçek yaşam verilerine dayalı olarak oluşturulan iki örnek vaka çalışması üzerinde gösterilmiştir. Sonuçlar, bu faktörlerdeki belirsizliğin karar alma sürecine dahil edilmesinin, politika yapıcıların daha etkili ve adapte olabilen stratejiler kullanmalarına olanak tanıyacağını ortaya koymaktadır. Ayrıca stokastik çözümün değeri bize parametrelerin sadece beklenen değerleri esas alınarak yapılan aşı dağıtımına göre salgın kontrolü açısından daha iyi bir çözüm elde edildiğini göstermektedir.

Anahtar sözcükler: Aşı dağıtımı, Stokastik programlama.

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Chapter 1

Introduction

In the early days of COVID-19 pandemic, the main strategy to stop or reduce the spread was implementing lockdowns. A global vaccine development progress began slightly after these isolation policies. A widespread distribution of vaccines aimed to reduce the disease spread through herd immunity, which results in fewer new infections over time. To achieve this, the World Health Organization released several guidelines for global vaccination strategies [1].

Since 2020, a large number of initiatives for vaccine development have been started. Nevertheless, only a small number of vaccines have effectively advanced through all three testing stages to become eligible for use in humans (see details in [2]).

An important factor slowing down the COVID-19 vaccine mass production was the availability of raw materials [3]. Shortage of the materials and equipment caused delays in scaling-up the vaccine production [4]. Such challenges in the COVID-19 vaccine development and production phases resulted in a scarce supply of vaccines during the early days of vaccine roll-out campaigns. Moreover, due to the complexity of the vaccine distribution supply chain there are many challenges to overcome to effectively distribute vaccines globally. For example, Biontech vaccine required a cold chain transportation, which leads to higher costs for some

countries that do not have enough infrastructure [5].

The COVID-19 pandemic has brought the issue of vaccine allocation under scarce supply to the forefront of public health discussions. With limited supplies of vaccines available, it is crucial to ensure that these valuable resources are distributed in a fair and efficient manner. As the vaccines are being distributed, the question of how to prioritize and allocate the limited supply becomes critical to ensure that the most vulnerable people are protected while considering the overall welfare of the society. Moreover, the problem involves uncertain factors such as the spread dynamics, vaccine efficacy and the amount of supply that will be available, which makes it even more challenging.

Motivated by this, the current study aims to investigate the challenges and potential solutions for allocating COVID-19 vaccines under scarce supply. We propose novel stochastic programming (SP) models to incorporate uncertainty, especially regarding the mutations, disease spread dynamics and vaccine supply.

The rest of the thesis is organized as follows. In Chapter 2, we review the relevant studies that address the vaccine allocation problem using Operational Research (OR) methods. In Chapter 3, we give the problem definition and the mathematical models that we formulate for the allocation problem. In Chapter 4, we solve our model with real life data and obtain results. Lastly in Chapter 5, we discuss future extensions of our work.

Chapter 2

Literature Review

In this Chapter, we review some of the recent literature on different vaccine allocation problems and the corresponding disease spread models. There is a vast amount of studies considering different variants of the vaccine allocation problem. In Table 2.1, we list some recent studies that focus on vaccine allocation decisions for diseases such as flu, Ebola, and recently, COVID-19. In almost all of these models, the main decision variables are vaccination rates of different population subgroups. Most studies assume that a single vaccine type is available while in some studies, there are different types of vaccines. The majority of the vaccine allocation models has single objectives in their problem settings while in some of them equity concerns are also addressed.

We discuss the related literature in two parts. We first discuss the vaccine allocation models then mention the methodologies used to incorporate disease spread dynamics into these mathematical models.

Table 2.1: Recent studies from the literature

Article	Objective	Vaccine Type	Case	Disease Model	Math. Model Type
[6]	Min Cost	Single	Flu	Stochastic SEIR	2 Stage Stochastic
[7]	Min total vaccine, equity	Single	Influenza	Next Generation Matrix	Non-linear
[8]	Max health benefit	Single	-	SIR	Diff equation
[9]	Min	Two/ Multiple Dose	-	SIR	Diff equation
[10]	CCNDP	Single	-	Network	Graph
[11]		Single	Flu	Agent based vs SEIR	Non-linear
[12]	Min death	Single	Smallpox	SIR	MIP
[13]	Min death	Single	Smallpox	SEIR	
[14]	Min cost	Single	Influenza	Simulation based	
[15]	Min cost	Food distribution	Influenza	Simulation based	MIP
[16]	Resource allocation	Two type (H,L)	COVID-19	SIR	
[17]	Bi-objective	Multi type	COVID-19		Non-linear MIP
[18]	Multi-objective		COVID-19		IP
[19]	Min infections, equity , Resource allocation		Ebola	SIR	Stochastic multi stage
[20]	Min infections , Resource allocation		Ebola	SIR	MIP
[21]	Min infection, risk averse, Resource allocation		Ebola	SIR	Stochastic
Our 2 Stage SP Models	Max Health Benefits with equity	Single	COVID-19	Next Generation Matrix	Non-linear

2.1 Vaccine Allocation Problems

The vaccine allocation problem is a special type of resource allocation problem that arises in disease related settings. The OR literature has offered solutions to this important planning problem through various optimization frameworks. We will mention some of the recent examples that are relevant to the problem that we consider.

[6] construct a two stage stochastic programming problem for vaccine allocations. In their setting, vaccination is done in two phases aiming to minimize the vaccination costs in the first stage and expected vaccination costs in the second stage.

[7] consider a vaccine allocation problem for influenza disease. They minimize total vaccine distributions subject to disease control in a deterministic setting, considering equity constraints. They construct sub-population groups based on age and allow interactions between each other when it comes to disease spread. Their model has non-linear constraints related to the next generation matrix disease control mechanism. They apply McCormick envelopes to solve their model efficiently.

When the types of mathematical models are investigated, we see that [8] and [9] construct an analytical approach and derive closed-form solutions for the vaccine allocation problems. [9] consider the minimization of the final size of the outbreak subject to budget constraint. In their study, there are two vaccines that have different efficacy levels against the disease. They compare several vaccination strategies. One vaccine type has more efficacy but is expensive at the same time. The other one is cheaper but has less efficacy. [8] also study analytical approaches in their vaccine allocation problem, where they maximize the herd effect of the vaccination. On the other hand, some studies obtain numerical results for their problems. A number of studies relied on solving mixed integer programming problems ([12],[15],[20],[17]). Note that due to the need to incorporate spread dynamics, most of these models are nonlinear.

[10] work on a generic network problem and they apply it to disease spread settings. They study cardinality-constrained critical node detection problem (CC-NDP). They remove critical nodes and obtain disconnected subgraphs. In their problem formulations, each vertex in the graph has a potential to become infected and infected vertices spread disease in the network. To minimize disease spread in the network, the critical nodes are removed while ensuring that disconnected subgraphs have a cardinality constraint for their vertices.

[11] compare agent based simulation models with compartmental models when it comes to disease control by vaccination. They consider four performance measures in their optimization setting, namely total cost, total number of infections, total number of deaths and total life year lost. They show that when the basic reproduction number is low and vaccine stocks are not very scarce, agent-based simulations perform better than compartmental models.

[12] consider smallpox outbreak. They minimize fatalities due to the smallpox outbreak considering resource constraints. To do so, they formulate a mixed integer programming problem. To control this disease spread they consider three different strategies namely isolation, ring vaccination and mass vaccination in different locations.

Several recent studies also consider a multi-objective approach to their problems. For example [17] work on a vaccine distribution problem. They construct a mixed integer nonlinear programming model with two objectives. One objective is to minimize total cost and the other one is to minimize total fatalities. They consider two-dose vaccinations in their study and define three subgroups. Unvaccinated, one dose vaccinated and two dose vaccinated people have interactions between them regarding to disease spread.

[18] also consider a multi objective setting for their vaccine allocation optimization problem. They apply a weighted sum approach for solving their multi-objective problem. They calculate the price of fairness for decision makers to assess different vaccination policies. Within the scope of their problem, there exists a trade-off between fairness and geographic diversity. Lastly, they try to find a balance considering different fairness and diversity levels to minimize total fatalities.

[20],[19], [21] consider the Ebola outbreak in their studies. [19] develop epidemics-logistic optimization model. Their objective is to minimize total deaths and infections with limited budget over a time horizon. They consider a compartmental model for their resource allocation setting. In their disease spread settings, they consider migration from other regions,which makes the SEIR model linear. They solve the resulting model using CPLEX. [19] extend [20] by a multi-stage stochastic programming model. They also add three equity concepts in their stochastic programming model, infection inequity, capacity inequity and prevalence inequity. Lastly, [21] introduce risk aversion in stochastic programming setting and extend the previous work on the Ebola disease resource allocation problem.

[15] study a food distribution problem for an influenza outbreak formulating it as a mixed integer programming. They use an agent-based simulation model to predict disease patterns and develop a continuous time stochastic model for their influenza setting. In their simulations, they consider a small number of people who interact such as householder and coworker. The aim is providing food distribution for those staying at home. They construct two solution policies,

namely static and dynamic update for this purpose.

2.2 Disease Spread Models

Main objective of the vaccine allocation is to reduce disease related negative outcomes (death, hospitalizations etc.) and if possible to control disease spread completely in the population. Given that the initial supply is scarce, decision-makers (DM) have to make prioritization decisions when doing so they have to rely on periodical (daily or weekly) disease statistics such as number of infected people or recovered people. En route to addressing this problem, researchers developed epidemic models to predict how the disease may evolve.

One key aspect of any vaccine allocation models is how disease spread is incorporated into mathematical model. Various methods have been used in the literature, which can be categorized into three main groups: *compartmental methods* that analyze the spread dynamics over a number of periods, *next-generation matrix method* that focuses on controlling the spread in the long run, and lastly *network models* that divide the population into nodes and consider disease spread dynamics in the vertices of the graph.

In compartmental models, the population is divided into several compartments. Figure 2.1 shows an example in which the population is divided into five compartments as Susceptible (S), Exposed (E), Infected (I), Quarantined (Q) and Recovered (R). Note that depending on the characteristics of the disease, the total number of compartments may change. Transition rates between compartments are disease specific. In Figure 2.1 we can see these rates (ω, η, α). The following set of differential equations characterize these transitions

$$S_i^{'} = -\eta_i S_i \tag{2.1}$$
$$E_i^{'} = \eta_i S_i - \omega_i E_i \tag{2.2}$$
$$Q_i^{'} = p_i \omega_i E_i - \alpha_i Q_i \tag{2.3}$$
$$I_i^{'} = (1 - p_i)\omega_i E_i - \alpha_i I_i \tag{2.4}$$
$$R_i^{'} = \alpha_i Q_i + \alpha_i I_i \tag{2.5}$$

where η_i represents the total occurrence of new infection rate in subgroup i and it is calculated as follows (see Table 3.1 for explanations of the disease spread parameters $\gamma, \beta, \lambda, \delta, p$)

$$\bar{\eta}_{ij} = \gamma_i \beta_{ij} (\lambda_j E_j + \delta_j I_j) \tag{2.6}$$
$$\eta_i = \sum_{j \in J} \bar{\eta}_{ij} \tag{2.7}$$

where γ and δ are susceptibility and infectiousness rates. α is the recovery rate and ω is the transition rate of exposed individuals into the infected stage.

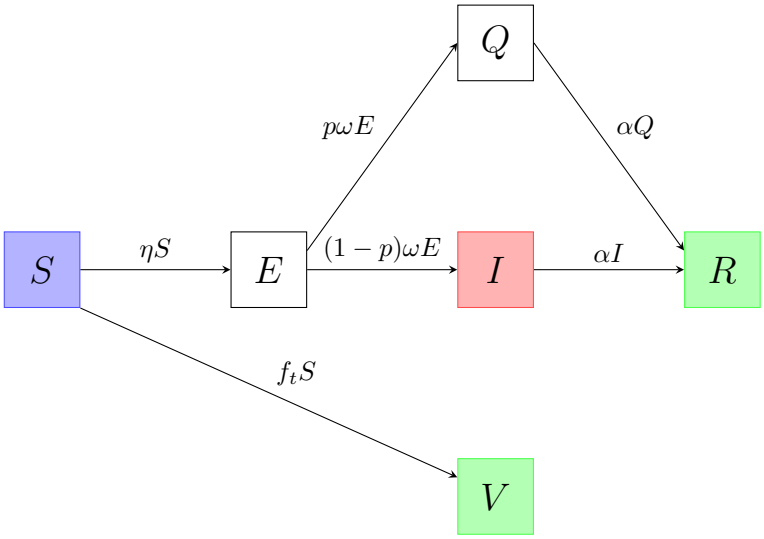


Figure 2.1: Compartments and transition rates.

Note that some studies consider the discretization of these nonlinear systems of differential equations, in a way that is similar to inventory-type constraints. At each time step, the number of people in each compartment is updated by a random or deterministic transition rate parameter.

Another way to include disease spread in any mathematical model is to construct a next-generation matrix K. The next-generation matrix explains the long-term behavior of the disease spread. To incorporate this method in the optimization framework we refer to [7] and follow their approach. The method relies on keeping the reproduction number R_f, which explains the overall secondary infections, below one. Hence in order to control disease spread while maximizing total health benefits, one can write a generic vaccine allocation optimization model as follows:

$$\max \sum_i b_i f_i n_i \tag{2.8}$$

$$\text{s.t.} R_f \leq 1 \tag{2.9}$$

$$f \in \mathcal{F} \tag{2.10}$$

It is difficult to consider constraint 2.9 directly in an optimization problem. For example, one can assume that a disease is controlled when the total infected people decreases over time, which can be achieved by either increasing the recovery rate of infected people or decreasing infection rate. In our stochastic programming settings we use an equivalent set of constraints to constraint 2.9 to control disease spread, based on the results of [22]. This set of constraints are also used in [7] and they rely on the so called next-generation matrix K. The elements of K_{ij}'s are calculated as follows

$$K_{ij} = \frac{\gamma_i \beta_{ij} \lambda_j}{\omega_j} + \frac{\gamma_i \beta_{ij} \delta_j (1 - p_j)}{\alpha_j} \tag{2.11}$$

where β is the contact rate between subgroups.

Denoting the vaccination rates as f_i for group i, let F be a diagonal matrix of vaccination rates, and ψ be the vaccine efficacy. One can construct the following matrix and use its spectral radius to control the spread [22]. Let D be a diagonal matrix, whose elements are equal to $1 - \psi f_i$.

$$(1 - \psi F)K = DK \tag{2.12}$$

This method allows us to calculate the distribution of the infected people after one generation by the following matrix multiplication. Let h be the initial infectious people in each subgroup, then

$$(DK)h = h^1$$

h^1 represents the infectious people in each subgroup after one generation. If we write this matrix multiplication several times, we will have the following expression.

$$(DK)^\ell h = h^\ell$$

where h^ℓ represents the infectious people in subgroups after ℓ generations. An infectious disease is controlled when h^ℓ becomes smaller in the long run. To ensure this, one can use eigenvalues of the DK matrix (See [22] for further details.).

$$h^\ell = (DK)^\ell h \tag{2.13}$$

$$= (DK)^\ell \sum_j c_j \chi_j \tag{2.14}$$

$$= \sum_j c_j \xi_j^\ell \chi_j \tag{2.15}$$

In our models, we also make use of these spread models, as will be detailed in the next Chapter.

Chapter 3

Problem Definition and Mathematical Models

We consider the vaccine allocation problem, in which a policy maker decides on the amounts to be allocated to various population groups, demanding a scarce supply. These population groups (or subgroups) could be defined with respect to various factors such as location, age or occupation. We assume that the decision maker has multiple concerns with different priorities: controlling the disease spread and if this is not possible for a community, maximizing benefit received from the vaccination. Meanwhile, as is the case in real life, we also consider fairness across the recipients. The stochastic programming models we constructed in this work aim to provide vaccine allocation solutions, considering the uncertainty in vaccine efficacy and disease spread factors due to the virus mutations. These models provide two-phase vaccination strategies, in which the first and second phase allocations are made before and after uncertain factors are revealed, respectively.

New variants of the disease may occur, which may lead to changes in the efficacy of the vaccines as well as the disease spread parameters. Motivated by this, we treat vaccine efficacy ψ as a random parameter and assume a two-stage decision-making setting, associated with first and second-stage variables f_{ij} and

y_{ij}^{ω}, respectively. These variables indicate the coverage in subgroups (i) of different regions (j).

In the following models, we consider vaccine allocation decisions that are made in two periods. The first period decisions aim to maximize disease control, which we quantify by utilizing the next generation matrix, as in [7], under uncertainty. In the second stage, the model allocates vaccines based on how the disease control is realized. We consider two variants of the model with respect to the objective of the second stage decisions. In the first one, we maximize benefits coming from vaccine allocations, while in the second one, we again maximize disease control.

A similar problem has been addressed in [6], which considered the vaccine allocation problem for the flu epidemic in two phases in geographically different regions. In their model, they minimize the vaccination cost at both stages. Note that our model is different than that of [6] in several ways. Their scenario generations are based on the disease status of the cities. They define a binomial random variable for each city to indicate whether in that city the disease is controlled or not. The probability distribution of this random variable is estimated by running simulations. In these simulations, they consider a minimum vaccination rate for each city and attack rate threshold (ART) for the disease. They perform 200 runs and calculate the percentage of the runs where number of infected individuals is less than ART, which they take as the probability of disease containment of a city given a minimum vaccination rate and ART. Unlike this study, we utilize the next generation matrix approach used in [7] to incorporate disease control into the optimization problem. The next-generation matrix method controls the long-term spread of the disease, i.e. ensures $R_0 \leq 1$. We extend the approach in [7] by incorporating uncertainty and allowing this constraint to be unsatisfied for some cities in some scenarios. The bilinear terms in this constraint make the mathematical model non-convex [7]. Hence, we use Gurobi Optimizer.

In the upcoming sections, we provide the formulations of our two stage stochastic programming models. Table 3.1 summarizes the notation we use in these models.

Table 3.1: Notation

	Symbol	Definition
Sets	I	set of subgroups
	J	set of regions
	Ω	set of scenarios
Indexes	i	subgroup
	j	region
	ω	scenario
Parameters	N_1	available vaccine doses in first stage
	N_2	available vaccine doses in second stage
	b	vaccine benefits
	n	subgroup populations
	γ	relative susceptibility of subgroups
	δ	relative infectiousness of infected individuals in subgroups
	β	contact rate between subgroups
	ψ	vaccine efficacy
	λ	infectiousness of exposed individuals in subgroups
	α	recovery rate
	p	quarantined proportion of exposed people
	M	a large number
Decision variables	f	first stage vaccine coverage
	v	eigenvector elements of the K matrix
	y	second stage vaccine coverage

3.1 Control-Benefit Model

Control-Benefit (CB) model aims to minimize disease spread in the first stage and then allocates vaccines to subgroups according to their welfare contributions in the second stage. Hence, the objective is to minimize total number of people in regions where the disease is not controlled and maximize health benefits.

We discuss this setting for a case, where the allocations are done across multiple geographical regions (cities) and across different age groups within these regions.

Note that this is without loss of generality, one can easily modify the formulation for different subgroup definitions. A simpler variant for example would consider groups defined based on age only for a single region, which could be a special case of our formulation.

In Figure 3.1 we can see the decision process. In the first stage, decision maker only knows available vaccine doses at the beginning for the first period. Accordingly they make vaccine allocation decisions f_{ij}, denoting the fraction of subgroup i of region j receiving vaccine. Then, we observe resolution of uncertainties ψ^ω, N_2^ω and K_{ij}^ω, which correspond to the efficacy, second period supply and the next generation matrix parameters, i.e. the spread dynamics. The binary variable z_j^ω, shows disease control in region j under scenario ω as a result of the first stage decisions. It is realized based on the efficacy and disease spread realizations and hence is known before the second stage allocations are made. Lastly, the decision maker decides which subgroups to vaccinate in the second stage, which is a recourse action denoted by the decision variable y_{ij}^ω. If disease is controlled in region j then there will be no vaccine allocations to this region. Our scenario set is Ω and probability of realization of each scenario is p^ω.

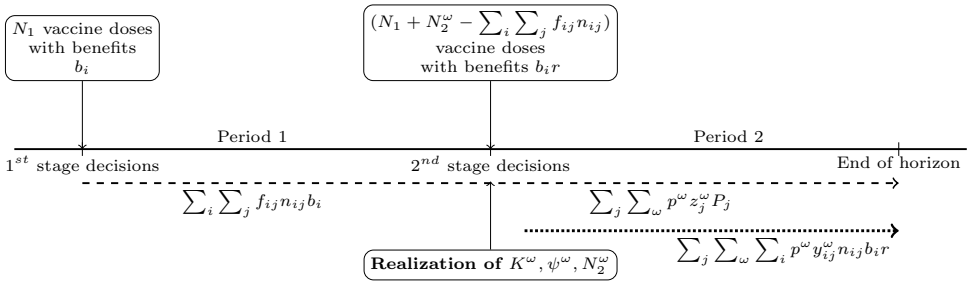


Figure 3.1: Two stage stochastic programming CB model.

$$\min \sum_{j\in J}\sum_{\omega\in\Omega} p^{\omega} z_j^{\omega} P_j \tag{3.1}$$

$$\max \sum_{j\in J}\sum_{i\in I} f_{ij} b_i n_{ij} \tag{3.2}$$

$$\max \sum_{j\in J}\sum_{\omega\in\Omega}\sum_{i\in I} p^{\omega} y_{ij}^{\omega} b_i r n_{ij} \tag{3.3}$$

$$\text{s.t} \sum_{j\in J}\sum_{i\in I} f_{ij} n_{ij} \leq N_1 \tag{3.4}$$

$$(1-\psi^{\omega} f_{ij}) \sum_{k\in I} K_{ik}^{\omega,j} v_k^{\omega,j} - M z_j^{\omega} \leq v_i^{\omega,j} \qquad \forall \omega \in \Omega, \forall i \in I, j \in J \tag{3.5}$$

$$\sum_{j\in J}\sum_{i\in I} n_{ij} y_{ij}^{\omega} \leq N_1 + N_2^{\omega} - \sum_{j\in J}\sum_{i\in I} f_{ij} n_{ij} \qquad \forall \omega \in \Omega \tag{3.6}$$

$$z_j^{\omega} f_{ij} + y_{ij}^{\omega} \leq z_j^{\omega} \qquad \forall \omega \in \Omega, \forall i \in I, \forall j \in J \tag{3.7}$$

$$\sum_{i\in I} v_i^{\omega,j} = 1 \qquad \forall \omega \in \Omega, \forall j \in J \tag{3.8}$$

$$0 \leq f_{ij} \leq 1 \qquad \forall i \in I \tag{3.9}$$

$$0 \leq y_{ij}^{\omega} \qquad \forall \omega \in \Omega, \forall i \in I \tag{3.10}$$

$$0 \leq v_i^{\omega,j} \leq 1 \qquad \forall \omega \in \Omega, \forall i \in I \tag{3.11}$$

The first objective minimizes sum of the product of city population ($P_j = \sum_{i\in I} n_{ij}$) and its corresponding binary variable. CB model tries to minimize this sum by allocating first stage vaccines to the cities. The second objective maximizes the total health benefits for all groups. The third objective aims to maximize benefit in regions where the disease is uncontrolled. We assume that the benefit received late is of less value; hence multiply the benefit parameter b_i with a constant r.

Constraint 3.4 is the capacity constraint, ensuring that the total amount of vaccines allocated in the first phase does not exceed the supply (N_1). Constraints 3.5 and 3.8 are the disease control constraints. They ensure that $z_j^{\omega} = 0$ when disease controlled in region j in scenario ω. Constraint 3.6 is the capacity constraint for the second stage allocations.

Note that, we use z_j^ω variables in constraint 3.7 to place an upper bound on our second stage decision variables. If disease is controlled in the first stage, we do not allocate any vaccines in the second stage. If disease is not controlled then we have the following upper bound $y_{ij}^\omega \leq 1 - f_{ij}$.

3.5 and 3.7 are nonlinear expressions due to the multiplication of f_{ij}'s and $v_k^{\omega,j}$'s and multiplication of f_{ij}'s and z_j^ω. We use Gurobi Optimization to deal with nonlinearity in 3.5. We can easily linearize 3.7 by adding following constraints in the CB model. Let $A_{ij}^\omega = z_j^\omega f_{ij}$, then we will have the following constraints in the model instead of 3.7

$$A_{ij}^\omega \leq z_j^\omega \qquad \forall i, j, \omega \tag{3.12}$$

$$A_{ij}^\omega \leq f_{ij} \qquad \forall i, j \tag{3.13}$$

$$A_{ij}^\omega \geq f_{ij} - 2(1 - z_j^\omega) \qquad \forall i, j \tag{3.14}$$

$$A_{ij}^\omega + y_{ij}^\omega \leq z_j^\omega \qquad \forall i, j, \omega \tag{3.15}$$

We use the lexicographic method. By doing so, we order the objective functions according to their importance level. In our case, minimization of $\sum_j \sum_\omega z_j^\omega P_j$ is prioritized. We first solve the problem L_1 and obtain the best value for the first objective, denoted as Δ_1^{opt}.

$$(\mathbf{L}_1) \min \sum_{j \in J} \sum_{\omega \in \Omega} z_j^\omega P_j \tag{3.16}$$

$$\text{s.t} 3.4 - 3.11 \tag{3.17}$$

Next we solve the following problem L_2. Again, we denote the optimal objective function value as Δ_2^{opt}.

$$(\mathbf{L}_2)\max \sum_{j\in J}\sum_{i\in I} f_{ij}b_i n_{ij} \tag{3.18}$$

$$\text{s.t}3.4-3.11 \tag{3.19}$$

$$\sum_{j\in J}\sum_{\omega\in\Omega} z_j^\omega P_j \leq \Delta_1^{opt} \tag{3.20}$$

Finally, we solve the following problem L_3 and obtain the final solution.

$$(\mathbf{L}_3)\max \sum_{j\in J}\sum_{\omega\in\Omega}\sum_{i\in I} p^\omega y_{ij}^\omega b_i r n_{ij} \tag{3.21}$$

$$\text{s.t}3.4-3.11 \tag{3.22}$$

$$\sum_{j\in J}\sum_{\omega\in\Omega} z_j^\omega P_j \leq \Delta_1^{opt} \tag{3.23}$$

$$\sum_{j\in J}\sum_{i\in I} f_{ij}b_i n_{ij} \geq \Delta_2^{opt} \tag{3.24}$$

To obtain equitable solutions across different geographical regions where the disease is uncontrolled after first stage decisions, we add the following constraint to the model

$$m^\omega = \sum_{j\in J} z_j^\omega$$

$$G^\omega = \frac{\sum_{j\in J}|\sum_{i\in I} z_j^\omega y_{ij}^\omega - \sum_{k\in I} z_j^\omega y_{kj}^\omega|}{2m^\omega \sum_{j\in J}\sum_{i\in I} z_j^\omega y_{ij}^\omega} \leq \epsilon$$

where G^ω is the Gini index for each scenario and m^ω is the sum of controlled

regions in that scenario. We linearize this constraint as follows

$$\sum_{i\in I} z_j^\omega y_{ij}^\omega - \sum_{k\in I} z_j^\omega y_{kj}^\omega \leq d_{ikj}^\omega$$
$$\sum_{k\in I} z_j^\omega y_{kj}^\omega - \sum_{i\in I} z_j^\omega y_{ij}^\omega \leq d_{ikj}^\omega$$
$$d_{ikj}^\omega = d_{kij}^\omega$$
$$\sum_{i\in I}\sum_{k\in I}\sum_{j\in J} d_{ikj}^\omega \leq 2m^\omega \epsilon \sum_{j\in J}\sum_{i\in I} z_j^\omega y_{ij}^\omega$$

Since we multiply y_{ij}^ω and z_j^ω we define an auxiliary variable F_{ij}^ω for this multiplication to make it linear [1]

$$\sum_{i\in I} F_{i,j}^\omega - \sum_{k\in I} F_{k,j}^\omega \leq d_{ikj}^\omega$$
$$\sum_{i\in I} F_{i,j}^\omega - \sum_{k\in I} F_{k,j}^\omega \leq d_{ikj}^\omega$$

3.2 Control-Control Model

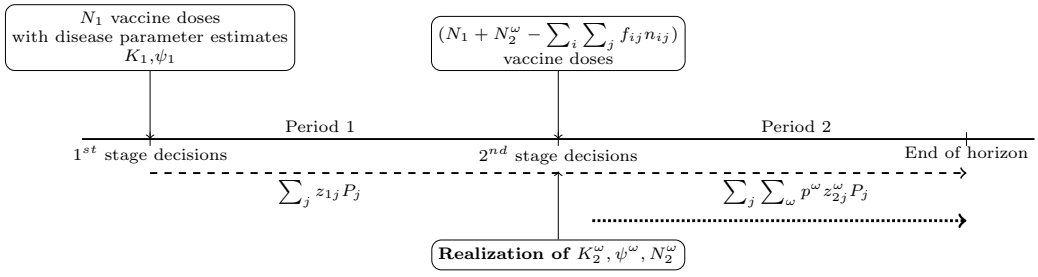


Figure 3.2: Two stage stochastic programming CC model.

Different from the previous model, we consider disease control mechanism in both stages. In Figure 3.2, we can see the general setting for this model. Initially, we

[1]Note that we still have multiplicative terms in the formulation due to m^ω being a decision variable. Nevertheless, as we already use the Gurobi solver setting the "NonConvex" parameter to 2, this does not cause an issue.

assume deterministic disease spread dynamics, K_1, and available vaccine doses N_1. We make our first stage allocation decisions f_{ij} and as a result disease control variables z_{1j}'s take their values. In the second stage, uncertainties about second stage vaccine availability, vaccine efficacy and disease spread realize. Then, we make our second stage decisions y_{ij}^{ω}. We aim to control disease spread in this model, hence use control maximization objective functions for both stages, measured by multiplying city populations with z_{1j} and z_{2j}^{ω} variables.

In the Control-Control (CC) model, we have first stage and second stage disease control constraints and hence have both z_{1j}, z_{2j}^{ω} variables. We assume a deterministic first stage next generation matrix (K_1) and stochastic second stage next generation matrix (K_2). Similar to Control-Benefit model, we solve the bi-objective model using lexicographic optimization.

$$\min \sum_j z_{1j} P_j \tag{3.25}$$

$$\min \sum_j \sum_{\omega} z_{2j}^{\omega} P_j \tag{3.26}$$

$$\text{s.t} 3.4, 3.9, 3.6, 3.10 \tag{3.27}$$

$$(1 - \psi_1 f_{ij}) \sum_k K_{ik}^j v_k^j - M z_{1j} \leq v_i^j \qquad \forall \omega \in \Omega, \forall i \in I, j \in J \tag{3.28}$$

$$z_{1j} f_{ij} + y_{ij}^{\omega} \leq z_{1j} \qquad \forall \omega \in \Omega, \forall i \in I, \forall j \in J \tag{3.29}$$

$$z_{1j}((1 - \psi^{\omega}(f_{ij} + y_{ij}^{\omega}))) \sum_k K_{2ik}^{\omega,j} v_{2k}^{\omega,j} - M z_{2j}^{\omega} \leq v_{2i}^{\omega,j} \qquad \forall \omega \in \Omega, \forall i \in I, j \in J \tag{3.30}$$

$$\sum_i v_i^j = 1 \qquad \forall j \in J \tag{3.31}$$

$$\sum_i v_{2i}^{\omega,j} = 1 \qquad \forall \omega \in \Omega, \forall j \in J \tag{3.32}$$

Instead of previous constraints 3.5 and 3.7, we use 3.28 and 3.30. By doing so, first we try to control disease spread in the first stage then we allocate second stage vaccines to the regions where disease is not controlled yet. Since the objective functions minimize the total population residing in regions where the disease is uncontrolled, the model allocates vaccines in both stages to reduce the disease spread.

We need to linearize 3.29 as well. Let $A_{ij} = z_{1j} f_{ij}$. We replace 3.29 by the following

$$A_{ij} \leq z_{1j} \qquad \forall i, j \qquad (3.33)$$

$$A_{ij} \leq f_{ij} \qquad \forall i, j \qquad (3.34)$$

$$A_{ij} \geq f_{ij} - 2(1 - z_{1j}) \qquad \forall i, j \qquad (3.35)$$

$$A_{ij} + y_{ij}^{\omega} \leq z_{1j} \qquad \forall i, j, \omega \qquad (3.36)$$

Similar to constraint 3.29, we make the following linearization in 3.30, where $A_{ij\omega}^2 = z_{1j} y_{ij}^{\omega}$.

$$A_{ij\omega}^2 \leq z_{1j} \qquad \forall i, j \qquad (3.37)$$

$$A_{ij\omega}^2 \leq y_{ij}^{\omega} \qquad \forall i, j, \omega \qquad (3.38)$$

$$A_{ij\omega}^2 \geq y_{ij}^{\omega} - 2(1 - z_{1j}) \qquad \forall i, j, \omega \qquad (3.39)$$

Chapter 4

Case Study

4.1 Data

Our case study focuses on Turkey demographics. We gathered population data from the Turkish Statistical Institute. In Table 4.2, we can see the populations of subgroups that we used in our problem settings. We divide the total population into subgroups considering their age (15-24, 25-34, 35-44, 45-64 and 65+). We constructed our age groups, the contact matrix and next generation matrix as in [7]. For the disease related parameters we rely on recent literature. For example, a similar subgroup setting is used in [23] and we use their disease parameters in our study. We use the parameter values used in [24] to calculate next generation matrix.

To obtain health benefits for each subgroup we do the following steps. Following the work of [25], we obtain health benefits for specific subgroups based on their corresponding COVID-19 risk levels. This approach involves considering risk classifications for mortality and hospitalization across different age groups, utilizing data from the Centers for Disease Control and Prevention (CDC) [26].

In Table A.1, we can see these risk factors of COVID-19 for different age

groups. We can also use the Hospitalization column of Table A.1. Following the same steps we obtain b_{alt} values in Table A.2. Our age groups slightly differ from theirs so we did a weighted average for age groups to obtain the benefit values for our model. The impact of the disease varies asymmetrically across the population, which leads decision makers to implement diverse vaccination strategies that prioritize specific age groups. As a result, segmenting the population becomes essential, particularly in situations of limited vaccine availability. Governments applied various vaccine rollout plans. For example in Turkey, the health minister announced a priority list, according to which vaccines were allocated during the early phase of the vaccination campaign (see [27]).

4.2 Instances

We consider two different problem instances (cases) for testing our stochastic programming models. The nature of the problem is similar in both instances, we only construct subgroups differently. In the first case, population is divided into age based subgroups and we allocate vaccines to subgroups living in different cities. In the second case, we divide the population into subgroups according to their age and consider only one geographic region. We consider Ankara for our one-city age groups case.

Table 4.2 shows the population data that we used for Case 1. According to Turkish Statistical Institute, 67.9% , 14.8% and 17.3% of total population live in large cities, medium sized cities and urban areas, respectively. To come up with a representative example, we scaled the populations accordingly for the sample of cities we considered.

For disease spread related parameters we use the following values in Table 4.1. The contact matrix β is also a disease parameter when calculating the next generation matrix (K), which we set as in [7]. For our scenario generations, we consider three different K matrices (denoted as K_h, K_m and K_l), five levels of second stage vaccinations and three levels of vaccine efficacy.

Table 4.1: Parameters used to generate matrix K

	K_h	K_m	K_l
γ	1.80	1.40	1
δ	1.50	1	0.50
α	0.15	0.35	0.45
p	0.50	0.50	0.50

Table 4.2: City and age group populations for case 1

Age Groups	İstanbul	Ankara	İzmir	Bursa	Antalya
15-24	2350951	852618	577161	432151	367308
25-34	2689746	895706	654191	479208	402383
35-44	2764998	933837	719703	519782	450324
45-64	3627568	1406509	1164290	777773	669124
65+	1210866	555385	553378	321334	251256
Total	12644129	4644055	3668723	2530248	2140395

In our numerical analysis we assume that all scenarios are equally likely, i.e. p^ω's are equal. We present our results of 2 Stage SP models for two cases. We used three K matrices, three levels of efficacy (ψ) values and lastly five levels of the second stage supply (N_2) to construct our scenarios. We also assume that total vaccines available in the first stage is 40 % of the total population.

- Case 1 Multiple Cities-Age Subgroups
- Case 2 Single City-Age Subgroups

4.3 Case 1: Multiple Regions-Age Subgroups

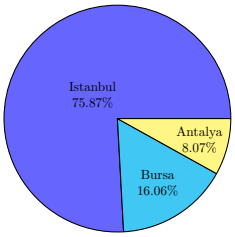
4.3.1 Control Benefit Model Results

We first solve Control-Benefit model and obtain first and second stage decisions for this problem. Figure 4.1a summarizes the first stage allocations, showing the amount of vaccines allocated to each city. It is seen that first stage vaccines are allocated to Istanbul, Bursa and Antalya. Istanbul is expected to receive the largest share due to its higher population. Our CB model gives priority to densely populated cities, as it aims to maximize the population in disease-controlled regions.

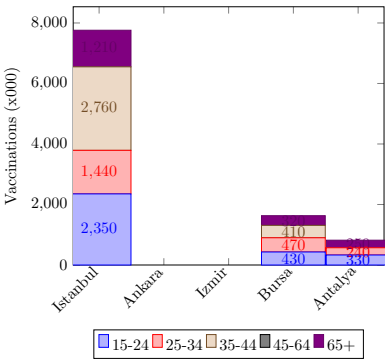
In Figure 4.1b we can observe the age groups that receive vaccine doses in the first stage. It is noticeable that relatively higher age groups (45-64 and 65+) receive a smaller proportion of the vaccines. This allocation is attributed to the CB model's focus on controlling disease spread in the first stage, followed by considering total health benefit received in the second stage. Disease transmission among younger people is more prominent than among the elderly in our context, which is consistent with the dynamics of the COVID-19. So in the first stage, vaccine allocation in Istanbul leads to complete vaccine coverage for 15-24 age group, 35-44 age group and 65+ age group. Then, about half of the 25-34 age group in Istanbul is vaccinated. In total, 61.5 % of Istanbul's population is vaccinated in the first stage. Figure 4.1b illustrates similar results for Bursa and Antalya. In Bursa the 15-24 age group is fully vaccinated, followed by almost everyone 25-34 age group. For 35-44 age group, approximately 410 thousand vaccines are allocated, covering around 80 % of this subgroup residing in Bursa. Lastly, the model allocates 320 thousand vaccines to 65+ age group, which corresponds to nearly the whole group. In Antalya, 330 , 240 and 250 thousand doses are allocated for the 15-24 and the 25-34 and 65+ age groups, resulting in vaccination coverage of 90 %, 60 %, and 100 %, respectively.

We observe that the first-stage vaccinations are allocated in a manner that results in Bursa and Antalya becoming controlled in optimistic scenario. Ankara

and Izmir receive no vaccine doses, since the model prioritizes disease control. In other words, the model emphasizes the importance of effectively controlling the spread in one city rather than allocating vaccines to another city if that will not be sufficient to control the disease.



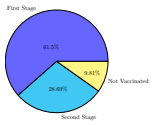
(a) First stage vaccine shares per city.



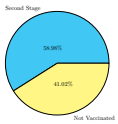
(b) Distribution to age groups.

Figure 4.1: First stage allocations case 1 CB model.

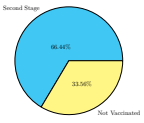
We then examine the second stage allocations for some sample scenarios. In Appendix B we provide the first and second stage results for an optimistic scenario. Figures 4.2-4.3 illustrate the second-stage allocations corresponding to medium and pessimistic scenarios, respectively. We provide information on whether the disease is controlled or not (C: Controlled, NC: Not controlled).



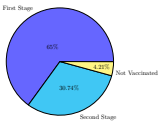
(a) Istanbul (NC).



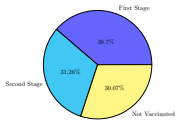
(b) Ankara (NC).



(c) Izmir (NC).

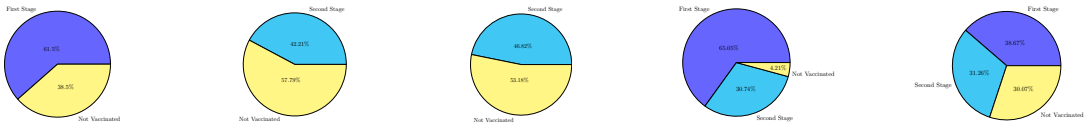


(d) Bursa (NC).



(e) Antalya (NC).

Figure 4.2: First and second stage allocations: case 1 CB, medium scenario (K_m, ψ =0.7, N_2=0.3).



(a) Istanbul (NC). (b) Ankara (NC). (c) Izmir (NC). (d) Bursa (NC). (e) Antalya (NC).

Figure 4.3: First and second stage allocations: case 1 CB, pessimistic scenario (K_h, ψ =0.5, N_2=0.2).

In the medium and pessimistic scenarios, slight changes can be observed in the allocation of second-stage vaccines, as depicted in Figures 4.2 and 4.3. The medium scenario sees a higher allocation of vaccines to Ankara and Izmir. In this case, first-stage vaccinations are unable to control the disease in any of the cities, leading to the allocation of second-stage vaccines across all of them. The coverage levels for each city are as follows: Istanbul at 29%, Ankara at 59%, Izmir at 66%, Bursa at 31%, and Antalya at 31%. In this scenario, the prioritization of second-stage vaccinations starts with elderly individuals and progresses to younger ones, guided by their elevated health benefits. As the disease persists beyond the first stage, the model allocates vaccines to the most vulnerable population in the second stage.

Similarly, in the pessimistic scenario, the effectiveness of first-stage vaccinations is insufficient to curb disease spread, owing to the lowest level of vaccine efficacy and a scenario of heightened disease transmission. Consequently, second-stage vaccinations are directed towards the elderly populations residing in Ankara, İzmir, Bursa, and Antalya. In this case, since the 65+ age group is already covered in the first stage for Bursa and Antalya, the second stage targets the 45-64 age groups in these cities. The coverage levels achieved through second-stage vaccinations are 42.21% for Ankara, 46.82% for İzmir, 30.74% for Bursa, and 31.26% for Antalya. Notably, Bursa achieves an overall coverage level of 95%, while Antalya reaches 70% coverage. In Table 4.3 and 4.4 we can see the coverage levels of age groups in the first stage and in the second stage.

Table 4.3: First stage coverage CB model case 1 (%)

	Istanbul	Bursa	Antalya
15-24	100	100	90
25-34	53	98	60
35-44	100	80	0
45-64	0	0	0
65+	100	100	100
Total	61.5	65	39

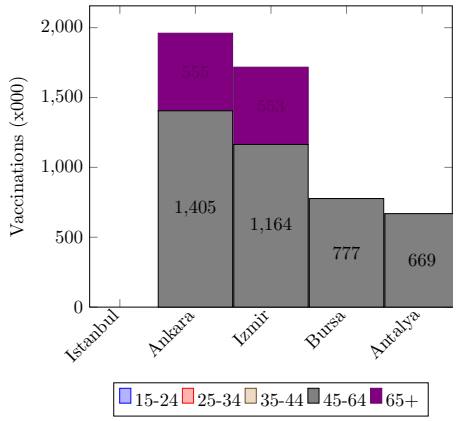
Table 4.4: Second stage coverage CB model case 1 (%)

	Istanbul		Ankara		Izmir		Bursa		Antalya	
	P	M	P	M	P	M	P	M	P	M
15-24	0	0	0	0	0	0	0	0	0	0
25-34	0	0	0	0	0	0	0	0	0	0
35-44	0	0	0	83	0	100	0	0	0	0
45-64	0	100	100	100	100	100	100	100	100	100
65+	0	0	100	100	100	100	0	0	0	0
Total	61.5	90	42	59	47	66	31	31	31	31

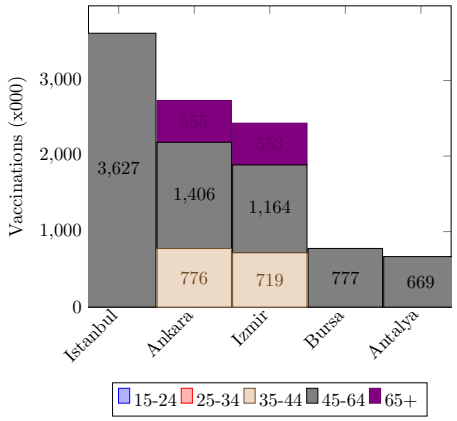
The main difference between medium scenario and pessimistic one is that Istanbul does not receive any second stage vaccinations in the pessimistic scenario as there is less vaccine supply. The model allocates the same amount of vaccines to Bursa and Antalya but fewer vaccines to Ankara and Izmir. This can be explained by the fact that health benefits for each subgroup in different cities are the same.

Overall, these observations highlight the dynamic adjustments the model makes in response to different scenarios, showing its adaptive nature in optimizing vaccine allocation and disease control outcomes. Decision makers can make the first stage allocations then observe the nature of the disease spread. Accordingly, they can make further allocations. This approach allows for a more

tailored and effective distribution strategy, ensuring that limited vaccine resources are maximally utilized.



(a) Second stage allocations pessimistic scenario CB, case 1.



(b) Second stage allocations medium scenario CB, case 1.

Figure 4.4: Second stage allocations CB case 1.

Figure 4.4a and 4.4b illustrate second stage allocations with respect to age groups for pessimistic and medium scenarios. While in the optimistic scenario the spread is controlled in all cities, rendering the second stage vaccinations unnecessary (see Appendix B); in medium (and hence the pessimistic) ones it is impossible to control disease spread in the first stage. Since the model allocates vaccines according to health benefits of the subgroups in the second stage, priority is given to elderly people who live in the uncontrolled cities. The CB model allocates same amount of vaccines to 45-64 and 65+ age groups in Ankara, Izmir, Bursa and Antalya in both scenarios. Since the 65+ age group in Istanbul is vaccinated in the first stage, CB model does not allocate vaccines to Istanbul in pessimistic scenario. Note that the health benefits for the 45-64 age group is same among the 5 cities. Therefore, our allocation strategy is to cover fully 45-64 age group in Bursa and Antalya instead of implementing further vaccination in Istanbul.

It is important to note that only 20 % of the total population receives second stage vaccinations in the pessimistic scenario. If the disease cannot be controlled

through the first stage allocations, then vaccines are allocated starting from the 65+ age group to younger subgroups. Moreover vaccines are allocated to fully cover one subgroup instead of partially covering the same age population in different cities.

As we can observe from Figure 4.4b, in the medium scenario, we observe Istanbul receiving second-stage vaccinations due to the greater vaccine supply available, as assumed for this scenario. These additional vaccines are allocated, beginning with the 45-64 age group in Istanbul, ensuring full coverage for this subgroup. Subsequently, CB model directs second-stage vaccines towards the 35-44 age group in Ankara and Izmir. Given the vaccination of the 35-44 age group in Istanbul, our second-stage strategy prioritizes the vaccination of the same age group in the most densely populated cities, rather than distributing them between Bursa and Antalya.

Value of Stochastic Solution: In order to obtain Value of Stochastic Solution (VSS), we solve the so called Expected Value (EV) problem using expected values of the random parameters. Then, we solve the stochastic programming (SP) model fixing the first stage allocations obtained from EV (L2) and obtain expected result of using the EV solution (EEV). VSS is the difference between objective function values of SP model (RP) and EEV.

In the next Table 4.5 we see the objective function values for the CB model for Case 1 instance. We also add the EEV solution to assess the value of stochastic solution (VSS) of the CB model. Additionally, we compare the total number of uncontrolled regions (without considering their populations) in all scenarios. For the primary objective of minimizing the number of people in uncontrolled regions, the CB 2 Stage SP model is preferable as it takes into account the uncertainty for both stages as opposed to EEV model, where the first stage decisions are made with respect to expected values of random parameters. It is seen that the SP model makes decisions that are better with respect to the primary objective, i.e. controls the disease better. For our primary objective the value of stochastic solution VSS=EEV-RP is 3,891,043 which is approximately 33 % of RP.

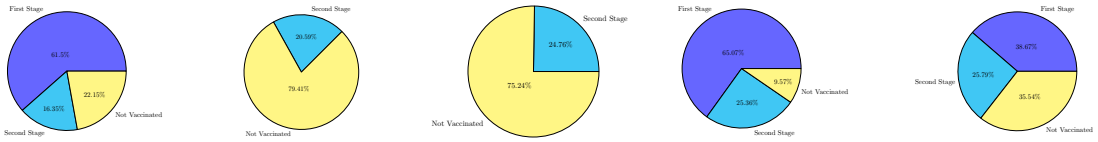
Note that we only maximize first stage benefits for the regions in which the disease can not be controlled given the first stage vaccinations. Since such uncontrolled cases is more in the EEV solution, the first stage benefits are higher. For the last objective where we calculate second stage benefits, the stochastic model also outperforms the EEV solution. Overall, the results verify that if we do not include randomness and solve only the EEV problem, we will have an inferior solution compared to the that of the SP model. The total number of uncontrolled regions is also less in the RP solution than the EEV solution. Again, it is due to considering uncertainty instead of taking only mean values for the random parameters. This shows the benefit of using the 2 stage stochastic programming model.

Table 4.5: Objective function values for control benefit model case 1

Criterion	RP	EEV
# of people in uncontrolled regions	11,551,265	15,442,308
Total first stage benefit in regions uncontrolled	154,054,622	291,787,923
Total second stage benefit in regions uncontrolled	54,387,155	26,843,317
$\sum_\omega \sum_j z_j^\omega$ (out of 225)	110	140

Incorporating Equity: Next, we present the results considering equity constraints for the CB model for Case 1. For Case 1, we define an equity constraint to allocate vaccines to subgroups who live in cities in the uncontrolled scenarios. Note that these equity constraints are related with the second stage allocations, hence first stage decisions stay the same. Moreover, in optimistic and medium scenarios, the allocations are similar with equity and without equity constraints. We put these results in Appendix B. In the optimistic scenario, we observe the same second stage results when we consider equity; because in this scenario, the disease is already controlled with first stage vaccine decisions. For the medium scenario, we also observe similar results. As the second stage vaccine allocation is not scarce and the model allocates vaccines in a balanced manner across cities. Lastly, in the pessimistic scenario second stage vaccine availability is very limited; hence solutions with and without equity considerations are significantly different. For this reason, we only discuss pessimistic scenario results, which are seen in

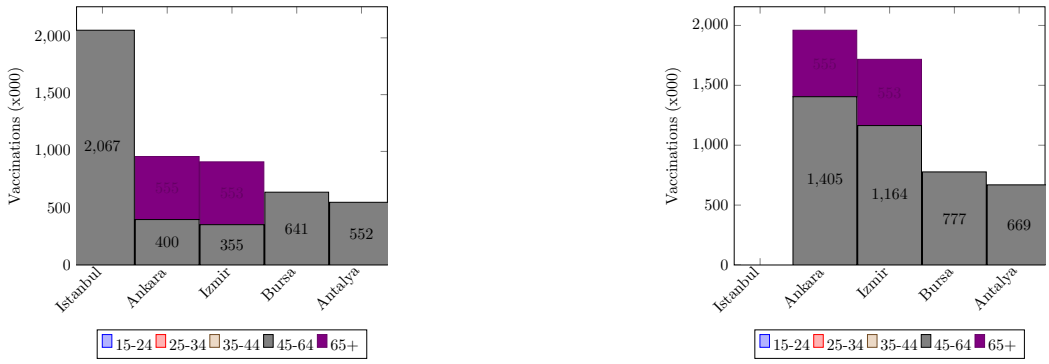
Figure 4.5.



(a) Istanbul. (b) Ankara. (c) Izmir. (d) Bursa. (e) Antalya

Figure 4.5: First and second stage allocations, case 1 CB, pessimistic scenario with fairness constraint (K_h, ψ =0.5, N_2=0.2,$\epsilon = 0.3$).

Recall that we use the ϵ parameter to control Gini coefficient level. The problem becomes infeasible when ϵ is very low (when $\epsilon = 0.2$). As we can see from Figure 4.5,as opposed to CB model without considering equity, Istanbul receives second stage vaccinations to cover 16 % of its population, which results in the others receiving less when there is equity concern between cities. This is also seen in detail in Figure 4.4a.



(a) Second stage allocations pessimistic scenario CB, case 1 gini.

(b) Second stage allocations pessimistic scenario CB, case 1.

Figure 4.6: Second stage allocations CB model with and without fairness constraint, case 1.

From the perspective of policy makers, the results with equity constraints can serve as a valuable tool to guide vaccine allocation strategies in instances where a pessimistic scenario materializes during the second stage. In such cases, the equity constraint encourages partial vaccination of age groups across different

cities. In Table 4.6, we can observe the age coverage of five cities for the CB model with equity constraint.

Table 4.6: Second stage coverage CB with fairness case 1 (%)

	Istanbul	Ankara	Izmir	Bursa	Antalya
	2nd Stage (P)	2nd Stage (P)	2nd Stage (P)	2nd Stage (P)	2nd Stage (P)
15-24	0	0	0	0	0
25-34	0	0	0	0	0
35-44	0	0	0	0	0
45-64	56	28	30	82	82
65+	0	100	100	0	0
Total	16	21	25	25	26

As expected, ensuring fairness results in a decrease in the overall total benefit. Table 4.7 shows the objective function values of CB model with equity constraints for Case 1 and without equity consideration, in which we see the decline in the total second stage benefit. The difference between the two can be considered as the price of equity in this case.

Table 4.7: Comparison of CB results with and without fairness constraints

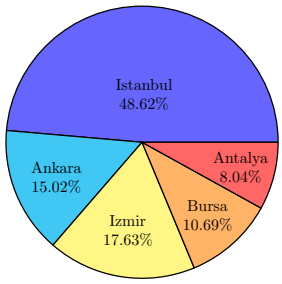
Criterion	RP (Gini)	RP
# of people in uncontrolled regions	11,551,265	11,551,265
Total first stage benefit in regions uncontrolled	154,054,622	154,054,622
Total second stage benefit in regions uncontrolled	30,714,685	54,387,155
$\sum_{\omega} \sum_{j} z_j^{\omega}$ (out of 225)	110	110

4.3.2 Control Control Model Results

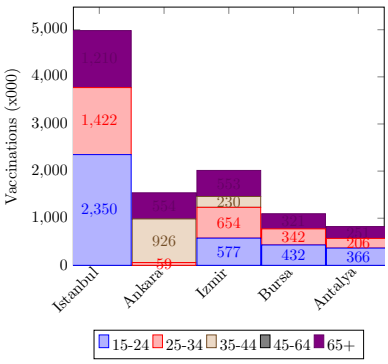
We then solve the Control-Control (CC) model for Case 1 with same parameter values. Recall that the main difference between the two models (CB - CC) is that the latter has disease control variables in both stages and aims to minimize the total number of people in disease uncontrolled regions both in the first and

second stages. Hence the CC model makes first stage allocations considering an additional next generation matrix K_1, which is deterministic.

Figure 4.7a illustrates the first stage vaccine shares per city obtained in the CC model. Istanbul receives the largest allocation at 48%, followed by Izmir at 17%, and Ankara at 15%. Bursa gets 11% of the allocation, while Antalya receives the smallest portion at 8%. In Figure 4.7b and Table 4.8 we see the first stage vaccinations and coverage of age groups, respectively. As the first stage allocations are done so as to control disease spread given K_1, we observe that CC model prioritizes young groups more compared to CB model. For the same reason, we also see that the first stage vaccines are more evenly allocated between cities.



(a) First stage vaccine shares per City CC, Case 1.



(b) First stage allocations age groups CC case 1.

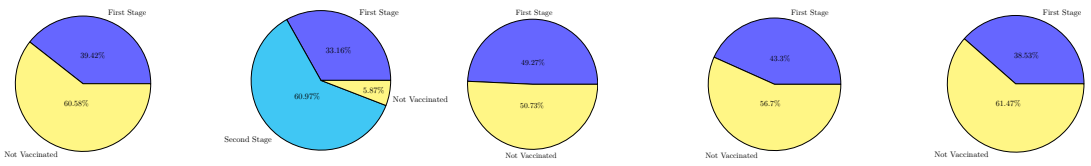
Figure 4.7: First stage allocations CC case 1.

Table 4.8: First stage coverage CC case 1 (%)

	Istanbul	Ankara	Izmir	Bursa	Antalya
15-24	100	0	100	100	100
25-34	52	5	100	71	51
35-44	0	99	31	0	0
45-64	0	0	0	0	0
65+	100	100	100	100	100
Total	39	33	49	43	39

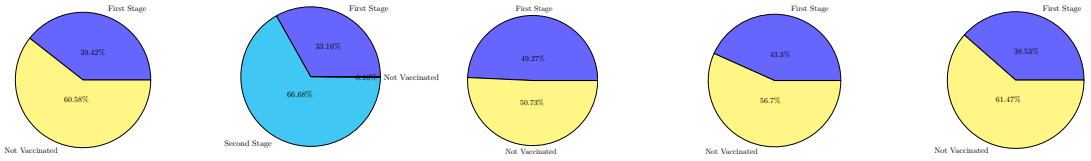
We can see from Figure 4.7b and Table 4.8, that compared to CB model (see Figure 4.1b) the CC model does not allocate vaccines to 35-44 age group in Istanbul and Bursa. Moreover, as 25-34 age group has the highest transmission rate, vaccines are allocated to this subgroup in every city to control disease spread. Again, due to the its higher population, most of the vaccines in the first stage is allocated to Istanbul.

In the second stage, vaccines are allocated to the cities where disease control is not achieved after first stage vaccinations. In this setting, only Ankara stays uncontrolled after the first stage allocation. Figure 4.8, illustrates results per cities for medium scenario. We provide the optimistic scenario results in Appendix C.



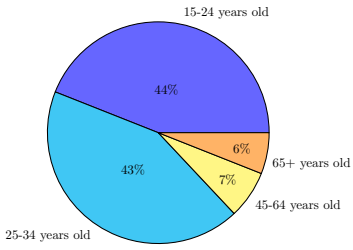
(a) Istanbul (FS). (b) Ankara (SS Cont.). (c) Izmir (FS). (d) Bursa (FS). (e) Antalya (FS).

Figure 4.8: First and second stage allocations case 1 CC medium scenario (K_m, ψ =0.7, N_2=0.3).

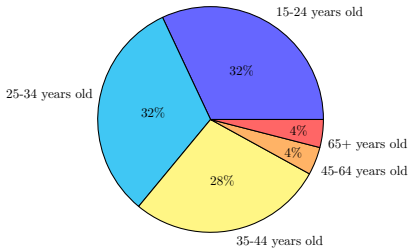


(a) Istanbul. (b) Ankara. (c) Izmir. (d) Bursa. (e) Antalya.

Figure 4.9: First and second stage allocations case 1 CC pessimistic scenario (K_h, ψ = 0.5, N_2=0.2).



(a) Second stage allocations in Ankara pessimistic scenario CC Case 1.



(b) Second stage allocation in Ankara medium scenario CC Case 1.

Figure 4.10: Second stage vaccinations for pessimistic and medium scenarios CC case 1.

In Figures 4.10a and 4.10b, we see the second stage solution for the pessimistic scenario and medium scenarios, respectively. Table 4.9 shows the age group coverage levels achieved with these allocations.

Table 4.9: CC model case 1 second stage coverage (%)

	Ankara	
	2nd Stage (P)	2nd Stage (M)
15-24	100	100
25-34	93	95
35-44	0	80
45-64	10	7
65+	20	20
Total	41	61

In both pessimistic and medium scenario, priority is given to young people as this decision will lead to disease free state at the end of the second stage. Although in medium case 35-44 age group receive a very large proportion of the vaccines, in the pessimistic scenario vaccines are not allocated to 35-44 age group. The model prefers to allocate vaccines to the same cities and same age groups if other possible allocation would not change the disease control status at the end

of the second stage.

Value of Stochastic Solution: In Table 4.10 we see the objective function values of the Control-Control (CC) model (RP) and the EEV model. We observe that the CC model objective values are better than the EEV results, which indicates that CC model control disease in first and second stage better than EEV model. For our primary objective the value of stochastic solution VSS=EEV-RP is 20,983,495 which is 450 % of RP.

Note that CC model focuses on disease control rather than considering health care benefits. Nevertheless, we also report the total benefit values of the RP and EEV solutions. We see that RP solution leads to lower health benefits. This is because young subgroups have more contact and transmission but the health benefits from vaccination are less compared to those of the elderly.

Table 4.10: Objective function values for CC case 1

Criterion	RP	EEV
# of people in uncontrolled regions 1st stage	4,644,055	25,627,550
# of people in uncontrolled regions 2nd stage	69,660,825	332,038,911
Total first stage benefit	188,593,299	219,750,738
Total second stage benefit in regions uncontrolled	11,073,302	12,964,208
$\sum_{\omega} \sum_{2j} z_j^{\omega}$ (out of 225)	15	67

4.4 Case 2: Single Region- Age Subgroups

4.4.1 Control Benefit Model Results

We now discuss the results for Case 2 whose population data is shown in Table 4.2. We consider a single city (Ankara) and the age groups in this city. As we have only one city in this setting, if the disease is controlled in a scenario, there will be no need for second stage vaccinations in that scenario. Figure 4.11 shows

the allocations per age groups in the Control Benefit model for Case 2. With these allocations, 11% of 35-44, 85% of 45-64 and 100% of 65+ subgroups can be vaccinated.

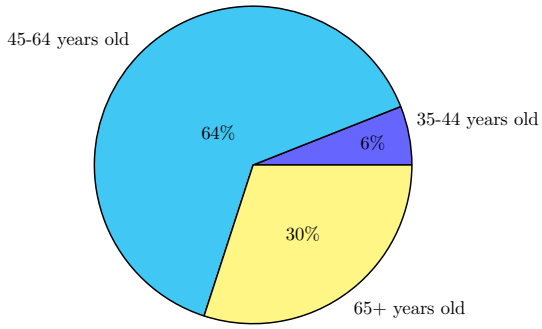
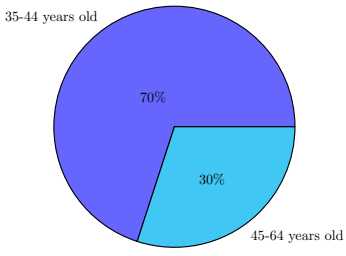
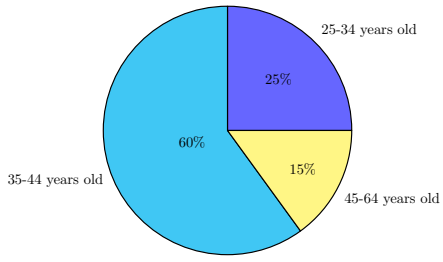


Figure 4.11: First stage allocations age groups case 2 CB model.

In Figures 4.14a and Figure 4.14b , we show the second stage vaccinations per age groups in the pessimistic ($N_2 = 20\%$ of the population, $\psi = 0.5$, K_h) and medium ($N_2 = 30\%$ of the population and $\psi = 0.7$, K_m) scenarios, respectively. This model becomes a continuous knapsack problem in the second stage when there is only one city and disease is not controlled in the first stage. Hence, it allocates second stage vaccines in an order, starting from older people as the vaccine related benefits are higher for these groups. Note that since 65+ group is totally vaccinated in the first stage, the allocation starts from the next age group of 45-64. In the medium scenario, as we can see from the Figure 4.14b that 25-34 group also gets vaccines as there is more supply.



(a) Second stage allocations per city CB case 2 pessimistic scenario



(b) Second stage allocations per city CB case 2 medium scenario

Figure 4.12: Second stage allocations CB case 2.

Value of Stochastic Solution: In Table 4.11, we see objective values of the lexicographic solution to the corresponding CB model. Similar to Case 1, we observe that CB model finds better results compared to the EEV model, where we obtain first stage solutions considering only expected values of the random parameters. First stage and second stage benefits are better in the EEV solution. However, according to our multi objective setting, objective functions are hierarchically important for us, hence the stochastic programming solution outperforms the EEV solution.

Table 4.11: Objective function values for CB case 2

Criterion	RP	EEV
# of people in disease-controlling scenarios	116,101,375	139,321,650
Total first stage benefit in regions uncontrolled	52,974,056	53,817,796
Total second stage benefit in regions uncontrolled	4,690,233	5,347,032
$\sum_{\omega} z^{\omega}$ (out of 45)	25	30

4.4.2 Control Control Model Results

Lastly, we solve the CC model for Case 2 vaccine allocations. Figure 4.13 shows the first stage vaccine allocations per age group. As opposed to CB model, for Case 1, CC model allocates vaccines 15-24 years old, 45-64 and 65+ years old.

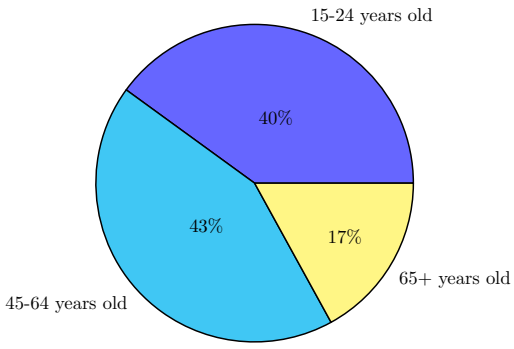
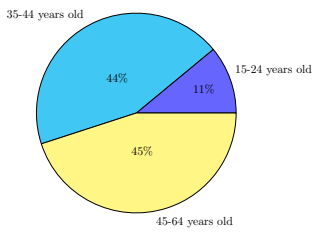
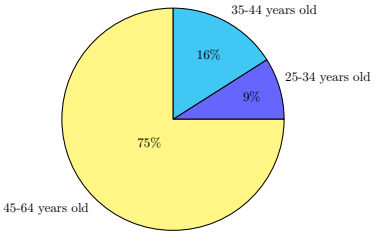


Figure 4.13: First stage allocation per age groups case 2 - CC model.



(a) Second stage allocations CC Case 2 pessimistic scenario.



(b) Second stage allocations CC Case 2 medium scenario.

Figure 4.14: Second stage allocations CC case 2.

Figure 4.14b illustrates the second stage allocations for pessimistic and medium scenarios. As expected, the CC model prioritizes younger groups to control disease spread in the second stage as much as possible. The difference between the pessimistic scenario and the medium one is that in the pessimistic scenario, 15-24 age group receives second stage vaccines however in the medium one this group does not receive any vaccine. This is due to the disease transmission dynamics. In the pessimistic scenario, since disease spread is assumed to be at its maximum level, 15-24 age group is prioritized due to their high interaction rate between other groups.

So, in the first stage, the model allocates vaccines in such a way that with additional second stage vaccinations the disease is under control in more scenarios.

For CB model, if disease spread can be controlled through the first stage allocations in all scenarios, then vaccines are allocated to age groups that have higher disease transmission rates in the first stage. If first stage allocations do not lead to disease control in all scenarios, then vaccines are allocated to the elderly people as well in the first stage. Because by doing so, the model reaches more second stage benefits for the second objective.

In the CC model, we focus on giving vaccines first to age groups that tend to spread the disease more. If we manage to control the disease effectively with the first batch of vaccines across all scenarios, we then direct more vaccines to younger age groups. But when the disease remains a challenge in all scenarios,

we mix up how we initially allocate vaccines. If we also focus on disease control in the second stage, then according to our results it is better to allocate vaccines to younger individuals.

Chapter 5

Conclusion

For diseases like COVID-19 that spread very quickly, vaccination is an effective strategy to control spread. As of August 2023 COVID-19 has been under control thanks to the world wide mass vaccination efforts. However, as seen in this recent pandemic, in the early phases of vaccination, additional strategies such as lockdown may also be necessary. In these phases, effective allocation strategies are key to avoid such undesired policies as much as possible. Motivated by this, we study the vaccine allocation problem under scarce supply.

This problem boils down to policy makers' deciding on the coverage of various population subgroups under various uncertain factors such as supply amount, disease spread dynamics and the vaccine efficacy. We formulate this problem using two two-stage stochastic programming models, which we call control-benefit and control-control based on the criteria used. We demonstrate usability our models on representative case studies that we constructed using population data. Our results show that both models have positive value of stochastic solutions. This indicates incorporating randomness in the model is significantly beneficial for vaccine allocations. Note that we use disease related data from COVID-19 for exemplary purposes but the framework can be easily adopted for other diseases.

The significance of this study lies in its potential to inform the development

of more effective vaccine allocation policies through providing valuable insights for policymakers and health officials. There are, however, some limitations to our work. The disease spread can be much complicated than we assumed in the models. We assume in the second model that once a region is controlled with respect to the corresponding next generation matrix, it will stay as controlled; i.e. the mutations will not increase the reproduction rate above the threshold.

We assumed a risk-neutral approach while a risk-averse one could also be used. An example would be extending the formulations using conditional value at risk (CVaR).Widely used health metrics such as quality-adjusted life years (QALY) could be incorporated into our models. Depending on the nature of the problem and the preferences of the policy makers, the objectives of the models can also be modified.

Bibliography

[1] WHO, "Global covid-19 vaccination strategy in a changing world: July 2022 update." https://www.who.int/publications/m/item/global-covid-19-vaccination-strategy-in-a-changing-world–july-2022-update. Accessed: 2022-07-10.

[2] S.-C. Wu, "Progress and concept for covid-19 vaccine development," *Biotechnology journal*, vol. 15, no. 6, 2020.

[3] HBR, "4 strategies to boost the global supply of covid-19 vaccines." https://hbr.org/2021/05/4-strategies-to-boost-the-global-supply-of-covid-19-vaccines. Accessed: 2023-08-23.

[4] C. P. Bown and T. J. Bollyky, "How covid-19 vaccine supply chains emerged in the midst of a pandemic," *The World Economy*, vol. 45, no. 2, pp. 468–522, 2022.

[5] 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, 2018.

[6] H. Yarmand, J. S. Ivy, B. Denton, and A. L. Lloyd, "Optimal two-phase vaccine allocation to geographically different regions under uncertainty," *European Journal of Operational Research*, vol. 233, no. 1, pp. 208–219, 2014.

[7] S. Enayati and O. Y. Özaltın, "Optimal influenza vaccine distribution with equity," *European Journal of Operational Research*, vol. 283, no. 2, pp. 714–725, 2020.

[8] L. E. Duijzer, W. L. van Jaarsveld, J. Wallinga, and R. Dekker, "Dose-optimal vaccine allocation over multiple populations," *Production and Operations Management*, vol. 27, no. 1, pp. 143–159, 2018.

[9] L. E. Duijzer, W. van Jaarsveld, and R. Dekker, "The benefits of combining early aspecific vaccination with later specific vaccination," *European Journal of Operational Research*, vol. 271, no. 2, pp. 606–619, 2018.

[10] M. Ventresca and D. Aleman, "A randomized algorithm with local search for containment of pandemic disease spread," *Computers & Operations Research*, vol. 48, pp. 11–19, 2014.

[11] O. O. Dalgıç, O. Y. Özaltın, W. A. Ciccotelli, and F. S. Erenay, "Deriving effective vaccine allocation strategies for pandemic influenza: Comparison of an agent-based simulation and a compartmental model," *PLOS ONE*, vol. 12, pp. 1–19, 02 2017.

[12] Y. Ren, F. Ordóñez, and S. Wu, "Optimal resource allocation response to a smallpox outbreak," *Computers & Industrial Engineering*, vol. 66, no. 2, pp. 325–337, 2013.

[13] O. Berman, A. Gavious, and M. B. Menezes, "Optimal response against bioterror attack on airport terminal," *European Journal of Operational Research*, vol. 219, no. 2, pp. 415–424, 2012.

[14] A. Uribe-Sánchez, A. Savachkin, A. Santana, D. Prieto-Santa, and T. K. Das, "A predictive decision-aid methodology for dynamic mitigation of influenza pandemics," *OR Spectrum*, vol. 33, pp. 751–786, 2011.

[15] A. Ekici, P. Keskinocak, and J. L. Swann, "Modeling influenza pandemic and planning food distribution," *Manufacturing & Service Operations Management*, vol. 16, no. 1, pp. 11–27, 2014.

[16] D. Kim, P. Pekgün, İnci Yildirim, and P. Keskinocak, "Resource allocation for different types of vaccines against covid-19: Tradeoffs and synergies between efficacy and reach," *Vaccine*, vol. 39, no. 47, pp. 6876–6882, 2021.

[17] M. Mohammadi, M. Dehghan, A. Pirayesh, and A. Dolgui, "Bi-objective optimization of a stochastic resilient vaccine distribution network in the context of the covid-19 pandemic," *Omega*, vol. 113, p. 102725, 2022.

[18] H. Anahideh, L. Kang, and N. Nezami, "Fair and diverse allocation of scarce resources," *Socio-Economic Planning Sciences*, vol. 80, p. 101193, 2022.

[19] X. Yin and I. E. Büyüktahtakın, "A multi-stage stochastic programming approach to epidemic resource allocation with equity considerations," *Health Care Management Science*, vol. 24, pp. 597–622, 2021.

[20] I. E. Büyüktahtakın, E. des Bordes, and E. Y. Kıbış, "A new epidemics–logistics model: Insights into controlling the ebola virus disease in west africa," *European Journal of Operational Research*, vol. 265, no. 3, pp. 1046–1063, 2018.

[21] X. Yin and I. E. Büyüktahtakın, "Risk-averse multi-stage stochastic programming to optimizing vaccine allocation and treatment logistics for effective epidemic response," *IISE Transactions on Healthcare Systems Engineering*, vol. 12, no. 1, pp. 52–74, 2022.

[22] A. N. Hill and I. M. Longini, "The critical vaccination fraction for heterogeneous epidemic models," *Mathematical Biosciences*, vol. 181, no. 1, pp. 85–106, 2003.

[23] P. Jarumaneeroj, P. O. Dusadeerungsikul, T. Chotivanich, T. Nopsopon, and K. Pongpirul, "An epidemiology-based model for the operational allocation of covid-19 vaccines: A case study of thailand," *Computers & Industrial Engineering*, vol. 167, p. 108031, 2022.

[24] X. Chen, M. Li, D. Simchi-Levi, and T. Zhao, "Allocation of covid-19 vaccines under limited supply," *SSRN Electronic Journal*, 2020.

[25] T. Breugem and L. N. Van Wassenhove, "The price of imposing vertical equity through asymmetric outcome constraints," *Management Science*, 2022.

[26] CDC, "Risk for covid-19 infection, hospitalization, and death by age group." https://stacks.cdc.gov/view/cdc/116835. Accessed: 2022-04-10.

[27] "List of covid-19 vaccination groups." https://covid19.saglik.gov.tr. Accessed: 2022-07-10.

Appendix A

Disease Spread Parameters

The contact rates between subgroups are given in the following equation. These subgroups are categorized as follows: 15-24, 25-34, 35-44, 45-64 and 65+ age groups. We refer to [7] for this contact matrix. When the contact rates are higher between subgroups, the disease tends to spread more among them. Our calculations of the next generation is based on the contact matrix, which affects the constraints on disease control.

$$\beta = \begin{bmatrix} 0.305 & 0.132 & 0.205 & 0.099 & 0.041 \\ 0.032 & 0.923 & 0.158 & 0.074 & 0.028 \\ 0.042 & 0.132 & 0.183 & 0.099 & 0.041 \\ 0.032 & 0.101 & 0.158 & 0.067 & 0.029 \\ 0.032 & 0.101 & 0.158 & 0.074 & 0.032 \end{bmatrix}$$

The impact of COVID-19 varies asymmetrically among individuals of different age groups, leading to distinct health outcomes for each subgroup. We refer to [26] for these risk factors of age groups. Table A.1 presents the risk factors associated with infection, hospitalization, and fatality rates across various age groups. Because our age groups are different than what is used in the literature, we adjusted these risk factors using the the population sizes. In our case studies,

we use vaccine benefits column of the Table A.2, which is the weighted average of hospitalization column of the A.1.

Table A.1: Risk for COVID-19 infection, hospitalization, and death by age group, CDC

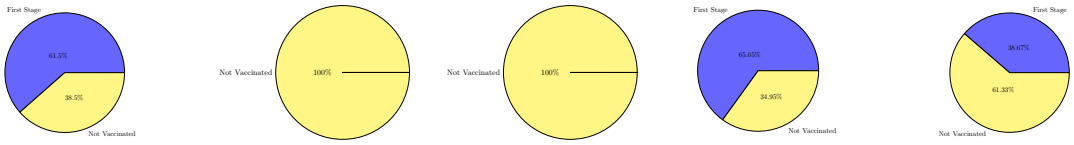
	Infection	Hospitalization	Death
0-4 years old	< 1	2	1
5-17 years old	1	1	1
18-29 years old	2	6	1
30-39 years old	2	10	4
40-49 years old	2	15	10
50-64 years old	2	25	25
65-74 years old	1	40	60
75-84 years old	1	65	140
85+ years old	2	95	340

Table A.2: Benefit values for different age groups

Age Groups	Vaccine Benefits
15-24	3
25-34	8
35-44	12
45-64	20
65+	50

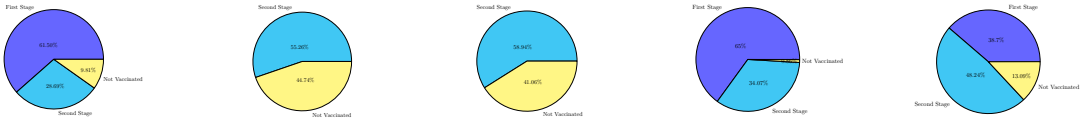
Appendix B

Detailed Results CB



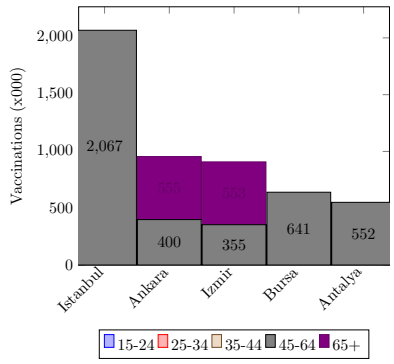
(a) Istanbul (FS Cont.) (b) Ankara (c) Izmir (d) Bursa (FS Cont.) (e) Antalya (FS Cont.).

Figure B.1: Allocations in an optimistic scenario case 1 CB model (K_l, ψ =0.9, N_2=0.4).

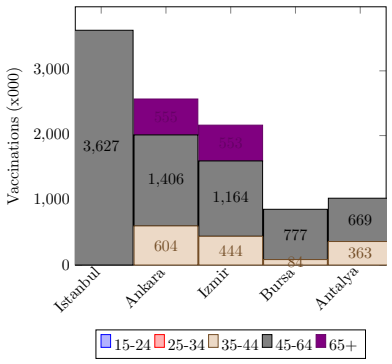


(a) Istanbul (b) Ankara (c) Izmir (d) Bursa (e) Antalya

Figure B.2: First and second stage allocations Case 1 CB medium scenario (K_m, ψ =0.7, N_2=0.3,$\epsilon = 0.3$)



(a) Second stage allocations pessimistic scenario CB case 1 gini.



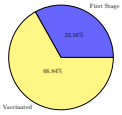
(b) Second stage allocations CB medium scenario case 1 gini.

Figure B.3: Second stage allocations CB gini case 1.

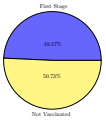
Appendix C

Detailed Results CC

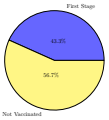
(a) Istanbul (FS Cont.)



(b) Ankara (FS Cont.)



(c) Izmir (FS Cont.)



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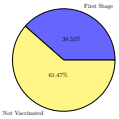
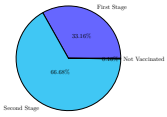


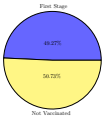
(e) Antalya (FS Cont.)

Figure C.1: First and second stage allocations case 1 CC scenario (K_l, ψ =0.9, N_2=0.4).

(a) Istanbul

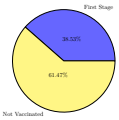


(b) Ankara



(c) Izmir

(d) Bursa



(e) Antalya

Figure C.2: First and second stage allocations case 1 CC scenario (K_h, ψ = 0.5, N_2=0.2).