

Optimal Resource Allocation Model to Mitigate the Impact of Pandemic Influenza: A Case Study for Turkey

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Abstract Pandemic influenza has been considered as a serious international health risk by many health authorities in the world. In mitigating pandemic influenza, effective allocation of limited health resources also plays a critical role along with effective use of medical prevention and treatment procedures. A national resource allocation program for prevention and treatment must be supported with the right allocation decisions for all regions and population risk groups. In this study, we develop a multi-objective mathematical programming model for optimal resource allocation decisions in a country where a serious risk of pandemic influenza may exist. These resources include monetary budget for antivirals and preventive vaccinations, Intensive Care Unit (ICU) beds, ventilators, and non-Intensive Care Unit (non-ICU) beds. The mathematical model has three objectives: minimization of number of deaths, number of cases and total morbidity days during a pandemic influenza. This model can be used as a decision support tool by decision makers to assess the impact of different scenarios such as attack rates, hospitalization and death ratios. These factors are found to be very influential on the allocation of the total budget among preventive vaccination, antiviral treatment and fixed resources. The data set collected from various sources for Turkey is used and analyzed in detail as a case study.

Keywords Pandemic influenza · Resource allocation · Multi-objective decision making · Turkey

Introduction

Pandemic diseases have become one of the most tragic events in human history. Although pandemic diseases have existed in every stage of the human history, the impact to humankind is more dramatic at some eras. For instance, it is estimated that 25 million of 100 million European population had died during the Black Death epidemic in Europe during 14th century. Despite the great advances in the prevention and treatment of epidemic diseases, pandemic diseases still pose a great threat to humankind. Pandemic influenza which has occurred intermittently over centuries and causing the millions of people deaths, social and economic impacts. Pandemic influenza occurred in 1918, 1957 and 1968; the pandemic of 1918 killed 20 million people worldwide [1]. Studies based on the past pandemics data estimate that the next pandemic influenza will have 15 to 35% gross clinical attack rate in the U.S. [2]. Gross clinical attack rate refers to the percentage of the population that becomes clinically ill due to an influenza pandemic. According to The U.S. National Intelligence Council's report, pandemic influenza is defined as the most important threat to the global economy [3]. Due to the severity of the risk posed by pandemic influenza, health planners are seeking the most appropriate interventions during an influenza pandemic in order to reduce number of cases, hospitalizations and deaths.

Interventions for pandemic influenza basically consist of surveillance, vaccination, communications, maintenance of necessary services and use of antivirals. Hence, planning for pandemic influenza is necessary to successfully strengthen the health care system's ability to respond and to efficiently allocate scarce intervention resources such as antiviral and vaccines.

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The literature on pandemic diseases can be classified into two main categories. The studies in the first category deal with mathematical modeling of the progression of an infectious disease within a population while the studies in the second category attempt to solve the resource allocation problem for epidemic and pandemic diseases.

The progression of infectious diseases can be modeled either by differential equations [4] and mathematical programming or by simulation. Flahault et al. [5] model the global diffusion of pandemic influenza and the impact of available preventive and control measure by using mathematical modeling. Lipsitch et al. [6] develop a deterministic compartmental model of the transmission of oseltamivir-sensitive and resistant influenza infections during a pandemic. Larson [7] studied influenza progression within a heterogeneous population using mathematical modeling. In a similar study, Ferguson et al. [8] proposed a mathematical model of influenza transmission dynamics and they used simulation modeling to analyze the impact of neuraminidase inhibitor therapy on infection rates and transmission of drug-resistant viral strains. As an example for stochastic modeling, Longini et al. [9, 10] developed a stochastic influenza simulation model to investigate the effectiveness of antiviral to contain influenza and compare targeted antiviral prophylaxis with vaccination strategies. Monte Carlo simulation is commonly used to estimate the impact of interventions during an influenza pandemic [11].

The literature on optimal resource allocation for epidemic and pandemic diseases is very diverse in terms of problem characteristics. Several linear and nonlinear optimization resource allocation approaches have been developed for the epidemic control. Resource allocation models are mostly for HIV/AIDS which is quite different from pandemic influenza in terms of time window to respond and seasonality. The resource allocation problem is usually stated as choosing the amount to be invested in several interventions to optimize total health benefits according to budget constraints [12]. Kaplan proposes a nonlinear dynamic programming method to maximize the number of averted HIV infections [13]. In another study for HIV, Zaric and Brandeau develop a multi-period resource allocation model for epidemic control programs using a dynamic compartmental model [14]. Dynamic compartmental models are common to model the spread of HIV under the condition where population changes over time and transitions to and from a compartment are typically defined by a system of dynamic equations [15, 16]. Another common modeling approach to allocate limited healthcare resources is linear programming [17, 18].

Based on our extensive literature review and to our knowledge there is no analytical study of resource allocation problem for pandemic influenza which is quite different from other resource allocation problems. There-

fore, this paper proposes a new multi-objective mathematical programming model especially for pandemic influenza.

Problem formulation

Pandemic influenza is inevitable according to many reports by CDC, WHO and medical experts across the world [19]. During and before an influenza pandemic, physical and human resources and budget for intervention are limited. Hence, an efficient resource allocation policy is crucial for public health and ability to respond this challenge in a timely manner.

In order to contain an influenza pandemic, control interventions include two strategies. The first one is a non-pharmaceutical approach such as social distancing and infection control and the other strategy is a pharmaceutical approach such as the use of influenza vaccines and antiviral for treatment and prophylaxis [20]. In this study, we focus on resource allocation for intervention methods such as antivirals and preventive vaccinations. Furthermore, the other resources such as intensive care unit, ventilators and hospital beds are also included in the model formulation.

In this proposed model, the overall region (which could be an entire country) is divided into regions and total population is divided into risk groups according to age and risk level. The mathematical model has three main objectives: (1) minimization of the number of deaths, (2) minimization of the number of cases, and (3) minimization of total morbidity days during a pandemic influenza.

The notation used for the mathematical formulation is summarized as follows:

Indices

i	region index ($i=1, \dots, m$)
j	risk group index ($j=1, \dots, n$)
r	fixed resource type index (1: intensive care beds; 2: non-intensive care beds; 3: ventilators) $r=1, \dots, k$

Input Parameters

P	total population in the overall region
P_{ij}	population of j th risk group in i th region
a_{ij}	probability of getting ill for patients not receiving preventive vaccines in j th subpopulation within i th region
β_{ij}	probability of getting ill for patients receiving preventive vaccines in j th risk group within i th region
λ_i	exposure rate of i th region
c_a	unit cost of antiviral drug treatment (USD/unit)
q_j	the amount of antiviral drugs used per patient in j th risk group
c_p	unit cost of preventive vaccine (USD/unit)

A_{ir}	available number of fixed resource type r in i th region
l_r	number of patients that can use fixed resource r during a pandemic period
d_{jr}	proportion of patients in j th risk group that will need fixed resource r (%)
B	total monetary budget (USD)
c_r	unit purchasing cost of fixed resource r
dr_j^+	mortality rate for patients in j th risk group receiving antiviral drug treatment (%)
dr_j^-	mortality rate for patients in j th risk group not receiving antiviral drug treatment (%)
ds_{jr}^+	mortality rate for patients of j th risk group that use fixed resource r (%)
ds_{ir}^-	mortality rate for patients in of i th region that do not use fixed resource r (%)
ts_{ij}^+	number of morbidity days of patients in i th region and in j th risk group receiving antiviral drug treatment
ts_{ij}^-	number of morbidity days of patients in i th region and in j th risk group not receiving antiviral drug treatment
md_{jr}^+	number of morbidity days of patients in j th risk group that use fixed resource r
md_r^-	number of morbidity days of patients that do not use fixed resource r

Decision Variables

TC_{AV}	total cost for antiviral treatment
TC_{PT}	total cost for preventive procedures
TCP_{FR}	total cost of purchasing additional fixed resources
TCU_{FR}	total usage cost of fixed resource r

Auxiliary Variables

x_{ij}	number of cases in risk group j in region i
AV_{ij}^+	the number of patients in risk group j in region i that receive antiviral drug treatment
AV_{ij}^-	the number of patients in risk group j in region i that do not receive antiviral drug treatment
P_{ij}^+	the number of patients in risk group j in region i that receive preventive procedures
P_{ij}^-	the number of patients in risk group j in region i that do not receive preventive procedures
a_{ir}	the additional number of fixed resource r purchased for region i
FR_{ir}^+	the number of patients in region i that use fixed resource r
FR_{ir}^-	the number of patients in region i that do not use fixed resource r
SFR_{ijr}	the number of patients in risk group j in region i that use fixed resource r

NG_{ijr}	the number people of risk group j in region i that need fixed resource r
NDR_{ir}	the number of fixed resource r that is needed in region i
c_{ir}	usage cost of fixed resource r in region i
TDA^+	total number of deaths for patients who receive antiviral drugs
TDA^-	total number of deaths for patients who do not receive antiviral drugs
TDS^+	total number of deaths for patients who use fixed resources
TDS^-	total number of deaths for patients who do not use fixed resource
TSA^+	total number of morbidity days of patients who receive antiviral drug treatment
TSA^-	total number of morbidity days of patients who do not receive antiviral drug treatment
TSS^+	total number of morbidity days of patients who use fixed resources
TSS^-	total number of morbidity days of patients who do not use fixed resources

As stated earlier, the model has the following three objective functions (see Eqs. 1–3). Since there are multiple objectives in the model, a hierarchical method for multi-objective optimization is used in order to generate optimal solutions.

i. *Minimization of the number of deaths*

$$\text{Min } z_1 = TDA^+ + TDA^- + TDS^+ + TDS^- \quad (1)$$

ii. *Minimization of the number of cases*

$$\text{Min } z_2 = \sum_{i=1}^m \sum_{j=1}^n x_{ij} \quad (2)$$

iii. *Minimization of morbidity days*

$$\text{Min } z_3 = TSA^+ + TSA^- + TSS^+ + TSS^- \quad (3)$$

The constraints and computational equations of the model are explained as follows. In Eq. (4), the number of cases are calculated by taking into account exposure rates of regions as well as the number of people taking preventive vaccination. This equation is based on the paper by Flessa [17, 18]. Equation (5) simply calculates the total antiviral cost and Eq. (6) ensures that the number of people receiving antiviral drugs does not exceed the total number of cases.

Calculation of the number of cases

$$x_{ij} = (\alpha_{ij}(P_{ij} - P_{ij}^+) + \beta_{ij}P_{ij}^+) * \lambda_i \quad (4)$$

$$i = 1, \dots, m; \quad j = 1, \dots, n$$

Calculation of total antiviral cost

$$TC_{AV} = c_a \sum_{i=1}^m \sum_{j=1}^n AV_{ij}^+ * q_j \tag{5}$$

$$AV_{ij}^+ \leq X_{ij} \tag{6}$$

Calculation of total cost of preventive procedures

$$TC_{PT} = c_p \sum_{i=1}^m \sum_{j=1}^n P_{ij}^+ \tag{7}$$

Equations (8) through (16) are related to fixed resources. The purchasing and usage cost of fixed resources are calculated in Eqs. (8) and (9) respectively. The number of people using a particular fixed resource type during a pandemic is calculated in Eq. (10) and quantities of fixed resources needed for cases are calculated in Eq. (11). Equation (12) calculates the number of people in risk group j in region i that use the fixed resource type r . Furthermore, Eq. (13) limits the number of people using the fixed resources by the quantity of the fixed resource available. The quantities of additional fixed resources that will be purchased is calculated in Eq. (14). The need for fixed resources is calculated in Eq. (15). Finally, the total budget constraint is expressed in Eq. (16).

Calculation of the total cost of purchasing additional fixed resources

$$TCP_{FR} = \sum_{i=1}^m \sum_{r=1}^k a_{ir} * c_r \tag{8}$$

Calculation of the total usage cost of fixed resources

$$TCU_{FR} = \sum_{i=1}^m \sum_{r=1}^k FR_{ir}^+ * c_{ir} \tag{9}$$

Calculation of the number of patients using fixed resources

$$FR_{ir}^+ = \min \left(\sum_j^N NG_{ijr}, (A_{ir} + a_{ir}) * l_r \right) \tag{10}$$

$i = 1, \dots, m \quad r = 1, \dots, k$

$$NG_{ijr} = X_{ij} * d_{jr} \quad i = 1, \dots, m \tag{11}$$

$j = 1, \dots, n \quad r = 1, \dots, k$

$$FR_{ir}^+ = \sum_{j=1}^n SFR_{ijr} \quad i = 1, \dots, m \quad r = 1, \dots, k \tag{12}$$

$$SFR_{ijr} \leq NG_{ijr} \quad i = 1, \dots, m \tag{13}$$

$$j = 1, \dots, n \quad r = 1, \dots, k$$

$$a_{ir} \leq \text{Max}((NDR_{ir} - A_{ir}), 0) \quad i = 1, \dots, m \tag{14}$$

$$r = 1, \dots, k$$

$$NDR_{ir} = \left(\sum_{j=1}^n NG_{ijr} \right) / l_r \quad i = 1, \dots, m \tag{15}$$

$$r = 1, \dots, k$$

$$TC_{PT} + TC_{AV} + TCP_{FR} + TCU_{FR} \leq B \tag{16}$$

Equations (17) through (21) are for calculating the number of deaths. Equations (17) and (18) calculate the number of deaths for patients receiving and not receiving the antiviral drug treatment respectively. Similarly, Eqs. (19) and (20) calculate the number of deaths for patients using and not using the fixed resources respectively. The number of people for whom a particular fixed resource is not assigned is calculated in Eq. (21).

Calculation of the number of deaths

$$TDA^+ = \sum_{i=1}^m \sum_{j=1}^n AV_{ij}^+ * dr_j^+ \tag{17}$$

$$TDA^- = \sum_{i=1}^m \sum_{j=1}^n (X_{ij} - AV_{ij}^+) * dr_j^- \tag{18}$$

$$TDS^+ = \sum_{i=1}^m \sum_{j=1}^n \sum_{r=1}^k SFR_{ijr} * ds_{jr}^+ \tag{19}$$

$$TDS^- = \sum_{i=1}^m \sum_{r=1}^k FR_{ir}^- * ds_{ir}^- \tag{20}$$

$$FR_{ir}^- = \max \left(\left(\sum_{j=1}^n NG_{ijr} \right) - ((A_{ir} + a_{ir}) * l_r), 0 \right) \tag{21}$$

$$i = 1, \dots, m \quad j = 1, \dots, n$$

Equations (22) through (25) calculate the total number of morbidity days of patients depending on whether or not

Table 1 Risk groups [2]

	High risk	Low risk
0–19 age	G1	G4
20–64 age	G2	G5
65+	G3	G6

Table 3 Assumed proportions of risk groups within the population [2]

Risk group	Assumed proportion (%)
G1	2.24
G2	8.32
G3	2.83
G4	32.88
G5	49.45
G6	4.25

they use specific treatment and fixed resources. For instance, Eqs. (22) and (23) are separate mathematical expressions for the total number of morbidity days of patients receiving and not receiving the antiviral drug treatment respectively. Similarly, Eqs. (24) and (25) calculate the total number of morbidity days separately for patients using and not using the fixed resources respectively.

Calculation of the morbidity days

$$TSA^+ = \sum_{i=1}^m \sum_{j=1}^n ts_{ij}^+ * AV_{ij}^+ \tag{22}$$

$$TSA^- = \sum_{i=1}^m \sum_{j=1}^n ts_{ij}^- * (X_{ij} - AV_{ij}^+) \tag{23}$$

$$TSS^+ = \sum_{i=1}^m \sum_{j=1}^n \sum_{r=1}^k (SFR_{ijr} * md_{jr}^+) \tag{24}$$

$$TSS^- = \sum_{i=1}^m \sum_{r=1}^k FR_{ir}^- * md_r^- \tag{25}$$

Case study

In order to demonstrate the use of the optimization model, the model is run for the data set collected from various sources for Turkey. Turkey is one of the high risk countries for pandemic influenza since it is in the path of various emigrating birds. There have been incidents of bird flu in Turkey in recent years. Therefore, Turkey is a suitable country to test our model. The regional populations and populations by age in each region are compiled from the

Table 2 Assumed distribution of population among risk groups by region [21]

Number of people according to the risk groups						
Regions	G1	G2	G3	G4	G5	G6
1	135,969	647,732	250,012	1,988,550	3,850,404	375,017
2	330,502	1,414,604	392,242	4,833,589	8,409,032	588,364
3	135,026	607,839	207,657	1,974,753	3,613,268	311,485
4	89,765	312,421	116,950	1,312,818	1,857,168	175,425
5	38,384	151,804	78,363	561,363	902,393	117,545
6	84,787	326,974	162,769	1,240,007	1,943,679	244,154
7	205,078	662,716	192,690	2,999,267	3,939,475	289,034
8	63,060	286,437	100,808	922,255	1,702,706	151,211
9	25,573	133,561	52,409	374,009	793,948	78,614
10	93,436	444,817	181,927	1,366,498	2,644,193	272,891
11	95,391	173,883	37,769	1,395,099	1,033,639	56,653
12	41,563	121,622	44,498	607,863	722,977	66,748
13	160,045	310,990	79,514	2,340,659	1,848,661	119,270
14	88,583	277,879	103,662	1,295,532	1,651,835	155,494

Table 4 Assumed data for the model parameters

Assumptions	
Average length of non-ICU hospital stay for influenza-related illness (days)	5
Average length of ICU hospital stay for influenza-related illness (days)	10
Average length of ventilator usage for influenza-related illness (days)	10
Average proportion of admitted influenza patients who will need ICU care (%)	10
Average proportion of admitted influenza patients who will need ventilators (%)	7.5
Average proportion of influenza deaths assumed to be hospitalized (%)	70

raw data published in the official website of the Turkish Statistical Institute [21]. The population in each region is classified into six risk groups in Table 1 as it is done in similar studies [2]. The population of each risk group by region is estimated based on the high and low risk proportions of age groups published by Meltzer et al. [2] (see Tables 2 and 3). The data in the paper by Zhang et al. [1] is also used for the mathematical model parameters of this study (see Table 4).

The mathematical model is run for three different scenarios in which hospitalization and death rates are changed from the best case to the worst case. These rates are taken from a study by Zhang et al. [1] and shown in Table 5. We assume that exposure rates and probabilities of

Table 5 Population-based rates (per 1,000 persons) of hospitalizations and death in an influenza pandemic [1]

Rate per 1,000 persons			
Influenza outcome	Optimistic	Most likely	Pessimistic
Hospitalizations			
High risk			
0–19 years old	2.10	2.90	9.00
20–64 years old	0.83		5.14
65+ years old	4.00		13.00
Non-high-risk			
0–19 years old	0.20	0.50	2.90
20–64 years old	0.18		2.75
65+ years old	1.50		3.00
Deaths			
High risk			
0–19 years old	0.13	0.22	7.65
20–64 years old	0.10		5.72
65+ years old	2.76		5.63
Non-high-risk			
0–19 years old	0.01	0.02	0.13
20–64 years old	0.03	0.04	0.09
65+ years old	0.28	0.42	0.54

Table 6 Assumed unit antiviral treatment and vaccine costs [2]

Risk groups	Unit antiviral treatment cost (USD per patient)	Unit vaccine cost (USD per person)
G1	26	21
G2	42	21
G3	41	21
G4	26	21
G5	36	21
G6	41	21

getting ill for people receiving preventive vaccines for all regions and risk groups are the same ($\lambda_i=1$, and $\beta_{ij}=0.1$). Furthermore, this study uses the unit antiviral treatment costs and unit vaccination costs according to risk groups published by Meltzer et al. [2] (see Table 6). Also, each scenario is analyzed for 10, 15 and 20 USD budget per person.

In this case study, there are three types of fixed resources: Intensive Care Unit (ICU) beds, non-Intensive Care Unit (Non-ICU) beds and ventilators. The current available quantities of these resources in each region are provided in Table 7. These numbers are obtained officially from the Health Ministry of Turkey.

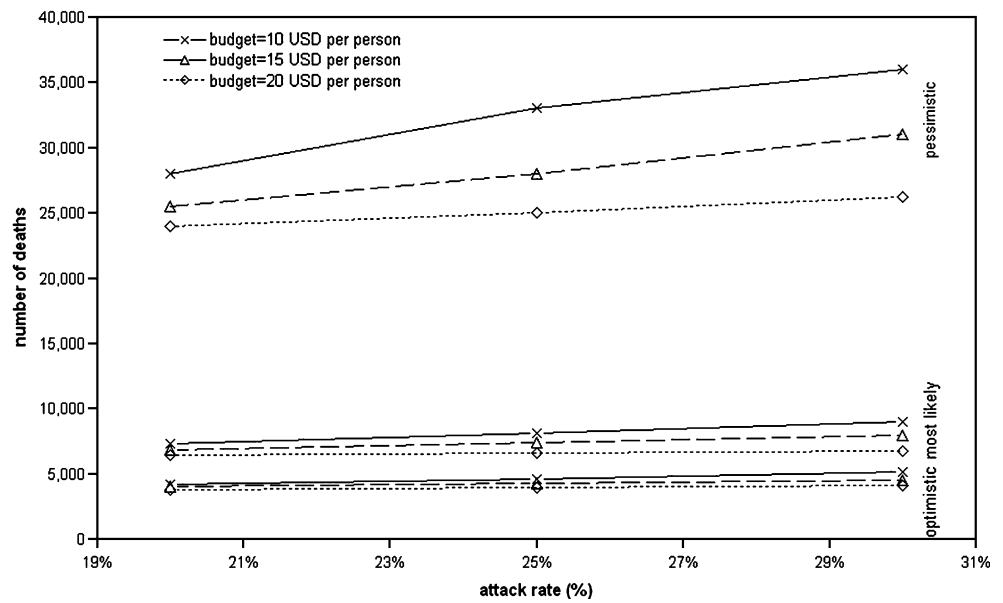
Results and discussion

The proposed model is solved using GAMS (General Algebraic Modeling System) optimization software's DNLP (Discontinuous Non Linear Program) solver. As stated earlier, a hierarchical multi-objective algorithm [22] is used to generate optimal solutions. In this algorithm, the

Table 7 Available fixed resource quantities in each region

Region no	Non-ICU beds	ICU beds	Ventilators
1	18,585	1,074	399
2	34,505	3,937	1,182
3	23,227	1,205	749
4	9,249	333	135
5	6,147	264	42
6	12,016	358	95
7	16,752	742	251
8	8,533	355	147
9	3,887	90	39
10	11,939	412	112
11	3,397	74	15
12	4,256	114	44
13	6,748	164	62
14	9,344	274	67

Fig. 1 Expected number of deaths under different scenarios



objective functions are ordered in terms of importance based on the preferences of the decision-maker. Then, the algorithm uses a multi-level reduced feasible region method. The algorithm at the first level attempts to minimize the objective function with the highest importance $f_1(x)$ over the feasible region outlined by the system constraints. The value of the objective function at the optimal point is used as a constraint for the next level optimization. At level 2, the objective function with second importance level $f_2(x)$ is minimized under the new constraint obtained from the first level. The algorithm continues in the same way for all objective functions. In our

formulation, the objective functions are in this importance order: (1) minimizing the number of deaths; (2) minimizing the number of cases; and (3) minimizing the total morbidity days.

In order to evaluate the impact of hospitalization and death rates on the optimal resource allocation solutions, three scenarios are taken into consideration as shown in Table 5. Also, three levels of attack rates (20, 25 and 30%) and three levels of budget per person (10, 15, 20 USD) are used in these model scenarios.

The expected number of deaths under these scenarios are shown in Fig. 1. There is a clear difference in the number of

Fig. 2 Expected number of cases under different scenarios

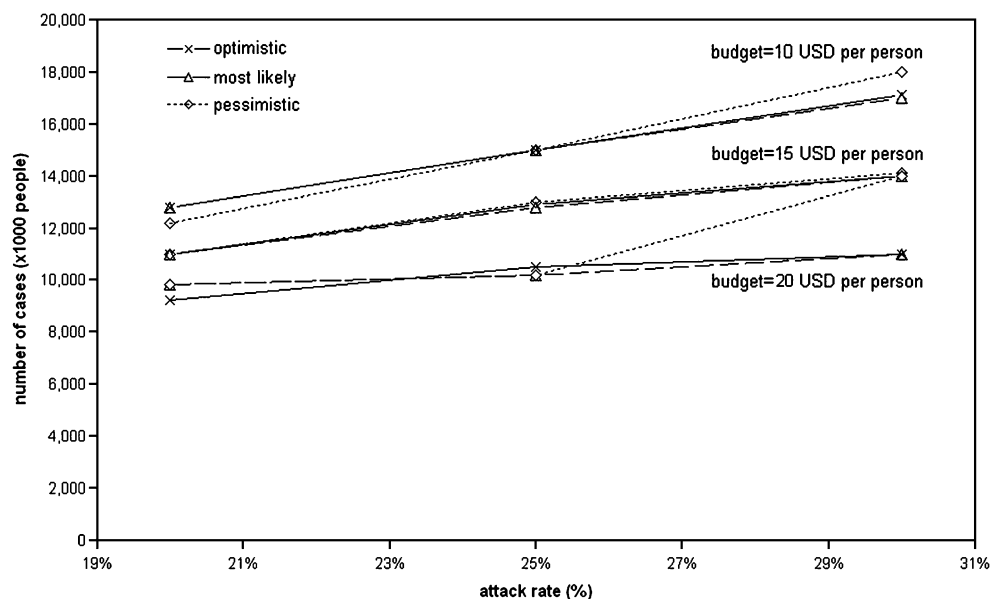
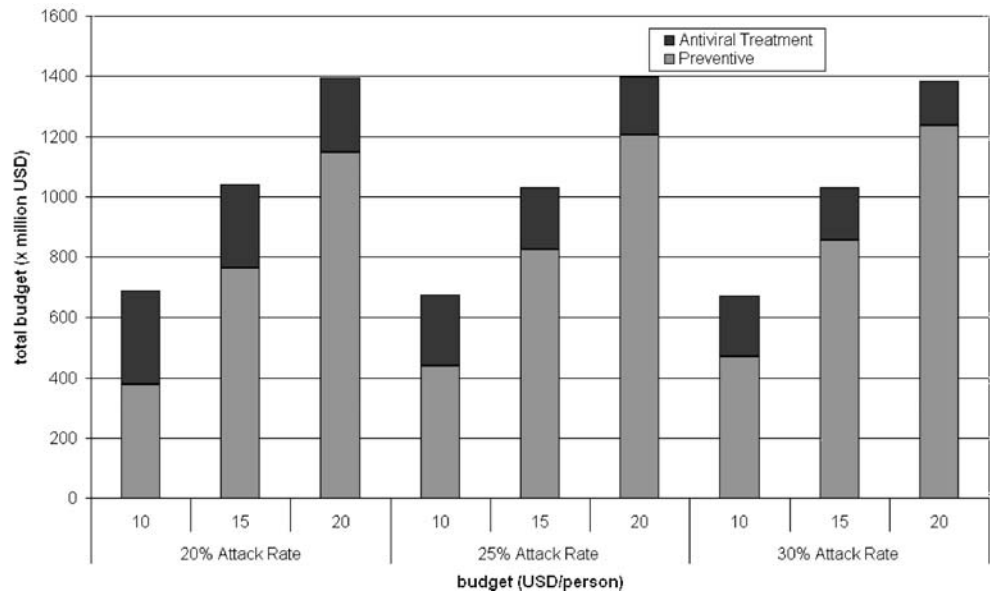


Fig. 3 Allocation of total budget among preventive vaccination and antiviral treatment under the optimistic scenario



deaths between the scenarios; especially, in the pessimistic scenario, the number of deaths are a lot larger than the other two scenarios as expected. Attack rate has the largest impact on the number of deaths in the pessimistic scenario. Furthermore, increasing the budget per person greatly reduces the number of deaths, especially in the pessimistic scenario.

On the other hand, Fig. 2 indicates that the budget per person is the most influential factor on the expected number of cases since the optimal solutions tend to allocate more monetary resources to preventive vaccinations in order to minimize potential deaths in case of an outbreak. When the attack rate is at the highest level in the pessimistic scenario and a large budget is available to mitigate a pandemic, the number of cases increases

sharply as the model allocates more budget to antiviral treatments and fixed resources, apart from the optimistic and most likely scenarios.

Allocation of total budget among preventive vaccination and antiviral treatment is illustrated in Fig. 3 for the optimistic scenario. As the attack rate gets higher, more budget is allocated to preventive vaccination to reduce both cases and deaths. Also, Fig. 4 illustrates the distribution of the total budget among regions of Turkey in terms of the money allocated per person. The regions with the darkest shading get the highest budget per person. The budget differences among the regions are mostly due to differences in demographic factors and healthcare infrastructure of the regions.

The distribution of cases among the risk groups under the most-likely scenario is shown in Fig. 5. Risk groups G4 and G5 have the highest number of cases since they are the largest risk groups in terms of number of people. On the other hand, the number of deaths is highest in G3 risk group (age 65+ and high risk) as shown in Fig. 6. Similar analyses can be made for other scenarios and factor combinations using the optimization model results.

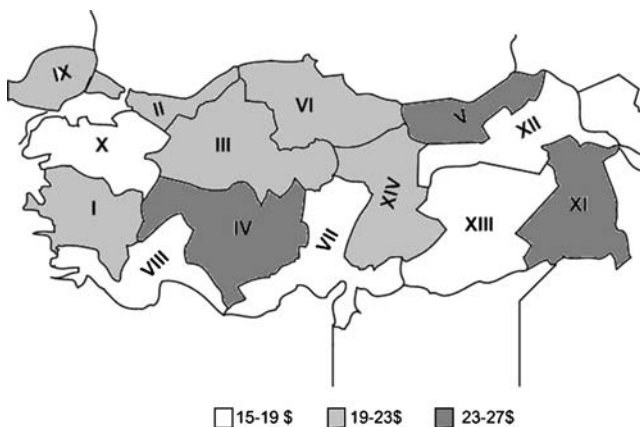
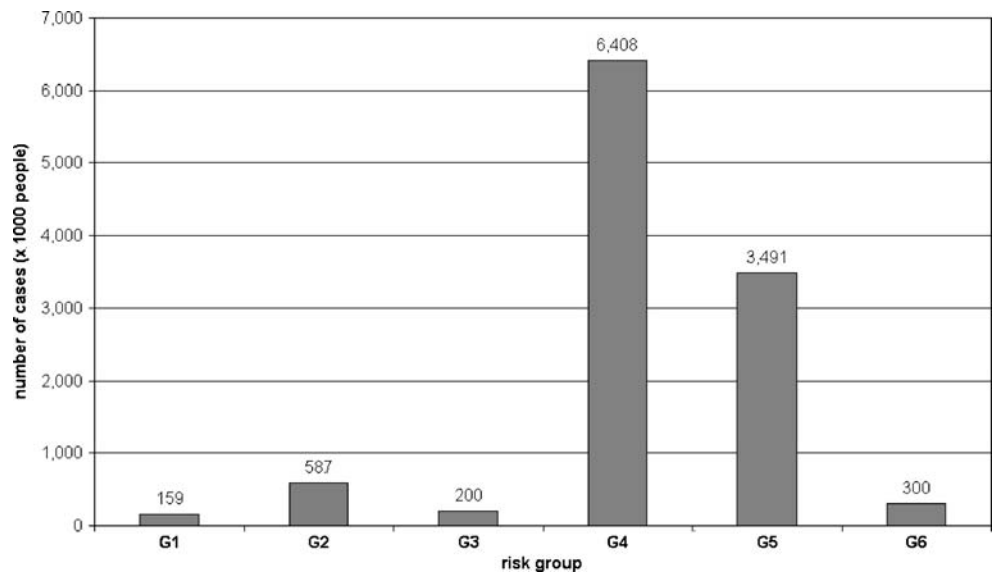


Fig. 4 Allocation of the total budget among regions of Turkey under the most likely scenario

Conclusions

In this study, we develop a multi-objective mathematical programming model that can be used to determine the optimal allocation of various types of resources among regions and risk groups of a country where a serious risk of pandemic influenza may exist. This model can be

Fig. 5 The distribution of cases among the risk groups under the most-likely scenario

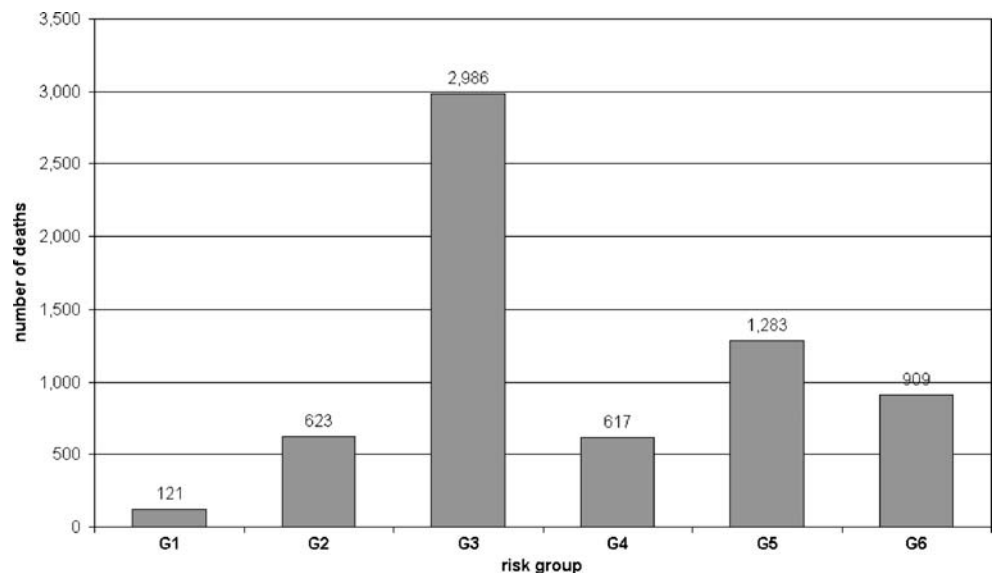


used as a decision support tool by decision makers to assess the impact of different scenarios such as attack rates, hospitalization ratio and death ratios. As a case study, the model is run for the data set collected from various sources for Turkey. The case study shows that attack rate, budget per person and the scenario level (optimistic, most likely, and pessimistic) are very influential on the allocation of the total budget among preventive vaccination, antiviral treatment and fixed resources. Optimal solutions tend to allocate most of

the budget to preventive vaccination and antiviral treatment rather than to the fixed resources.

As further study, the problem formulation can be made more realistic by considering some stochastic parameters such as the length of hospital stay, morbidity rates and costs. However, analytical modeling of such stochastic formulations is mathematically intractable in most cases. A simulation study would be a better approach to gain more insight into dynamics of a pandemic and resource allocation and dispatching policies under such uncertainties.

Fig. 6 The distribution of deaths among the risk groups under the most-likely scenario



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