Optimal Cholera Vaccine Allocation Policies in Developing Countries: A Case Study

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Abstract

Owing to the ongoing civil war, healthcare and sanitation systems have been destroyed, and the routine immunization activities have been interrupted in the country under consideration. In particular, around 70% of the population are under cholera threat according to World Health Organization. In addition to the improvement of hygiene and sanitation, and better access to clean and safe water, an effective allocation of oral cholera vaccines could help to prevent the spread of cholera. In this study, a mixed integer programming model is developed to identify the optimal number of cholera vaccines that need to be distributed for different age groups and regions based on the risk level of age groups and the population of regions. The objective is to maximize the percentage of individuals vaccinated against cholera while considering limited vaccine quantities constraint. Different vaccine allocation policies that consider age, population, and both age and population are used to allocate vaccine quantities among several age groups and regions. These policies are compared in terms of the number of individuals got vaccinated and the total vaccination cost. Based on findings, to opt among these policies, the decision makers should trade off between maximizing the population that should be vaccinated and minimizing the total vaccination cost.

Keywords: Mixed Integer Programming, Cholera, Optimal Vaccine Allocation

1. Introduction

Due to the ongoing civil war in Yemen, healthcare and sanitation systems have been destroyed, and the routine immunization activities have been interrupted. As a result, outbreak of cholera epidemic has reached alarming levels with millions of people impacted and thousands dead. According to World Health Organization (WHO) reports, 1,145,292 suspected cholera cases are cumulatively reported in Yemen from January 2018 to November 2019 with 1,507 associated death cases. Almost one third of stated cases have been reported in children under 5 years old. The regions reporting the highest number of suspected cases during 2019 are governorate of Alhudaydah with 118,158 cases, governorate of Sana'a with 101,027 cases, capital city Sana'a province with 95,208 cases, governorate of Hajjah with 70,388 cases, governorate of Ibb with 68,933 cases, governorate of Dhamar with 62,125 cases, and governorate of Amran with 47,359 cases (WHO EMRO | Outbreak update | Epidemic and pandemic diseases, 2019). United Nation (UN) reports state that more than 19 million of Yemeni people have not been able to obtain suitable healthcare, and more than 17 million do not have access for clean water (Cholera killed 3,000 Yemenis as needed vaccine didn't reach the nation, 2019). Those have formed the primary conditions for the spread of cholera, a disease that causes severe drying, vomiting and fever, and kills its victims rapidly if not treated.

In addition to improvement of hygiene and sanitation and access to clean and safe water, immunization with oral cholera vaccines (OCV) could play a significant role in long-term prevention and control of cholera outbreak.

Immunization using vaccine is a relatively new defense weapon against cholera spread, and until recent times it was only just delivered in emergency situations since production capacity for the vaccine was limited (Wise, 2018). The speed at which cholera spreads made targeting and allocating its vaccine a fuzzy decision; especially, when the available doses of the vaccine are limited and there are huge number of individuals are in need for vaccination. According to Yemen | Science | AAAS (2017), the foremost questions that encounter community health experts and international volunteers fighting the pervasive cholera epidemic in Yemen are who should be protected first, children or adults, and which regions should first be targeted to mitigate the cholera spread, wherein there is no local policy for determining the best allocation of cholera vaccine quantities available. In this study, a mixed integer programming model is developed to identify the optimal number of cholera vaccines that should be administrated for different age groups and regions. The aim is to maximize the percentage of population vaccinated against cholera throughout the regions reporting the highest number of suspected cholera cases in Yemen during 2019. Thereby mitigating the risk of cholera outbreak.

2. Literature Review

In the literature, several studies have been conducted to investigate the vaccine distribution and allocation problem for contagious and communicable diseases. Patel et al. (2005) integrated stochastic simulation with genetic algorithm to identify the optimal vaccine allocation strategy for influenza that minimizes the number of infections and deaths when the available quantities of the vaccine are limited. Another study conducted by Matrajt et al. (2013) employed mathematical modeling and genetic algorithm to find the best vaccine allocation for pandemic influenza. Their model aimed to minimize the infection attack rate given that the available vaccine quantities are limited. Jacobson et al. (1999) introduced an integer linear programming model to determine the quantities of vaccines that should be procured for a set of childhood diseases. The model aimed to minimize the cost of vaccine distribution based on vaccine types and quantities available for different combinations of diseases. Smalley et al. (2015) used mathematical modeling to find the optimal allocation strategy for delivering cholera vaccines in Bangladesh. Their study aimed to decrease the number of cholera cases. To this end, they developed a mixed integer programming model so as to find what quantities of vaccine are required, where, and when; thereby, minimizing disease incidence rate. Günay et al. (2019) developed a mathematical model to find the optimal quantities of vaccine required to maximize the percentage of Syrian refuges population vaccinated against polio in Turkey. On the other hand, other studies have been focused not only on the allocation strategies but also on the whole vaccine supply chains. Duijzer et al. (2018) conducted a comprehensive review for studies focusing on vaccine supply chains. They clustered them based on vaccine type, production problems addressed (e.g., vaccine production planning and scheduling, capacity problem of production resources), distribution and logistics issues such as inventory control policies, selection of distribution facility locations and the balancing problem of supply and demand for perishable vaccines. Other two review studies for research addressed the distribution part in vaccine supply chains were conducted by De Boeck et al. (2019) and Lemmens et al. (2016). All those review studies concluded that there is scarcity in studies concerning with operations research and management issues in vaccine supply chains such as scheduling problems for allocation policies of children vaccines. Other studies concentrated on evaluating the performance of vaccine supply chains in terms of mortality rate, shortage and holding cost, vaccine availability, amount of vaccines perished, percentage of population protected, etc. (Assi et al. 2013; Brown et al. 2014; Lee et al. 2015).

This study aims to develop a mixed-integer linear programming model. The objective is to maximize the percentage of individuals vaccinated against cholera given that there are limited doses of cholera vaccine. Different vaccine allocation policies that consider age, population, and both age and population are compared in terms of cost effectiveness and satisfying the objective function. This work is unique since it is inspired to solve a real-health problem that community health experts encounter in Yemen.

3. Problem Description and Model

The problem considered is how to allocate limited cholera vaccine doses over multiple age groups and regions. An optimization model is introduced to solve this problem. The model is applied to seven regions in Yemen that have reported the highest number of suspected cases of cholera during 2019. The population of these seven regions are classified based on age into two groups; namely, high risk age groups for children aged between 2 and 5 years old, and low risk age groups for individuals who are above 5 years. Vaccine allocation policies considered are (i) age-based policy where the priority is given for high risk age groups over low risk age groups since children have weak resistance for contagious diseases; (ii) region or population-based policy where the population of regions are taken into consideration while distributing vaccine quantities among regions. Accordingly, the region with higher population would receive larger quantities of vaccine without any prioritizing among age groups; (iii) age and population-based policy where both age group and population constraints are taken into account. According to WHO | Cholera (2019), the number of doses differs with respect to age of individuals. Thus, the cost of vaccination also depends on the age of a vaccine receiver. Primary immunization consists of three oral doses that need to be administrated to adults and children aged 6 years and over within two weeks. Children who are between 2–5 years old need to have two doses within minimum of one week and maximum of 6 weeks. Surprisingly, vaccination is not licensed for children under 2 years of age (WHO | Cholera 2019). If the second dose is delayed for more than 6 weeks, vaccination should be restarted afresh. In this study, it is assumed that each vaccinated individual receives the required doses without delay. The total cost per vaccinated individual is assumed to be \$6 (\$2/dose) for adults and children with 6 years old and over, and \$4 for children between 2-5 years. Dose cost includes vaccine cost of \$1.45, cost of \$.25 for customs, insurance and freight and \$.30 for delivery (Smalley et al. 2015). Table 1 introduces the population of the seven regions where the highest cholera cases have been reported according to the age groups. These statistics are based on projection for the most recent census conducted in 2004 (Yemen Population-Worldometer, 2020). The model helps determine the optimal quantity of vaccines for each age group and region considering limited doses of vaccine with the aim of maximizing the percentage of individuals receiving vaccination. The set, indices, parameters and decision variables of the proposed model are listed below.

Table 1: Projection of seven regions population based on the most recent census

Region	Population above 5 years old	Population between 2 and 5 years old
Capital city	1,937,451	222,806
Alhudaydah	3,774,914	434,115
Ibb	3,911,070	449,773
Sana’a	1,174,767	135,098
Hajjah	1,887,213	217,029
Dhamar	1,697,067	195,162
Amran	1,123,651	129,219

<u>Sets and indices</u>

I: set of regions, i = (Capital city, Alhudaydah, Ibb, Sana’a, Hajjah, Dhammar, Amran)

J: set of age groups, j = (2 – 5 years old, above 5 years)

<u>Parameters</u>

P: Overall population of all regions

p_i: Population of region *i*

p_{ij}: Population of region i age group *j*

c_j: Vaccination cost of an individual in age group *j*

n_j: Number of doses need to be administrated to an individual in age group *j*

Rh: Minimum ratio of individuals required to be vaccinated at high risk age group (2 – 5 years old)

Rl: Minimum ratio of individuals required to be vaccinated at low risk age group (above 5 years)

Q: Maximum available doses of vaccine for all regions

s: Unit shortage cost

<u>Variables</u>

y_{ij}: Number of individuals vaccinated in region *i* age group *j*

Model

$$Max \sum_{i\in I}\sum_{j\in J}\frac{y_{ij}}{P} \tag{1}$$

s.t.

$$\sum_{i\in I}\sum_{j\in J} n_j y_{ij} \leq Q \qquad \forall\, i \in I, j \in J \tag{2}$$

$$y_{ij} \leq p_{ij} \qquad \forall\, i \in I, j \in J \tag{3}$$

$$\frac{y_{ij}}{p_{ij}} \geq r_h \qquad \forall\, i \in I, j \text{ is high risk age group} \tag{4}$$

$$\frac{y_{ij}}{p_{ij}} \geq r_l \qquad \forall\, i \in I, j \text{ is low risk age group} \tag{5}$$

$$\sum_{j\in J} y_{ij} \geq \frac{p_i}{P}\sum_{i\in I}\sum_{j\in J} y_{ij} \qquad \forall\, i \in I \tag{6}$$

$$y_{ij} \in \mathbb{Z}^{+} \tag{7}$$

Equations (1)-(7) introduce the mixed integer programming model developed to solve the allocation problem of cholera vaccines in seven regions in Yemen. Equation (1) represents the objective function that maximizes the overall percentage of individuals vaccinated against cholera. Constraint (2) is to ensure that the total administered vaccines do not exceed the total available doses of vaccine. Constraint (3) guarantees that individuals vaccinated in region *i* age group *j* do not exceed the population in that group. Constraint (4) is to guarantee that the percentage of individuals vaccinated in region *i* at high risk age groups is greater than a minimum ratio, r_h. While constraint (5) is to ensure that the percentage of individuals vaccinated in region *i* at low risk age groups is greater than a minimum ratio, r_l. Constraints (4) and (5) are used to assign high priority for high risk age groups. Constraint (6) is used to allocate available vaccines among regions proportionally to the population of those regions; thereby, the higher population the region has, the larger quantities of vaccine the region receives. The number of vaccinated individuals must be a positive integer as restricted in constraint (7).

Total cost is used to compare the three allocation policies. The calculation of the total cost is introduced in Equation (8). It represents the summation of cost of doses delivered to each age group and region, $y_{ij}c_j$, which includes production cost of vaccine, customs, insurance and freight cost, and total shortage cost, Sc. Equations (9) introduces the calculation of the total shortage cost, which is computed by multiplying the number of individuals who are not vaccinated by unit shortage cost.

$$Tc = \sum_{i\in I}\sum_{j\in J} c_j y_{ij} + Sc \tag{8}$$

$$Sc = s\left(\sum_{i\in I}\sum_{j\in J} p_{ij} - y_{ij}\right) \tag{9}$$

Where Tc is the total cost, Sc is the total shortage cost, and s is the unit shortage cost

4. Numerical Results and Discussion

Three allocation policies are used to allocate vaccine quantities for different age groups and regions. The three policies are compared in terms of total number of individuals vaccinated and total and shortage costs. The total cost is mainly the cost of vaccine doses in addition to shortage cost. While the shortage cost is the number of individuals who are not vaccinated multiplied by shortage cost unit; which is assumed to be $0.2 per individual in this study. In region-based policy, the maximum available quantity of vaccine is allocated based on only the population of regions without prioritizing age groups within a region. Figure 1 shows the total number of individuals vaccinated in the seven regions and the optimal vaccine quantity allocated for each region based on region-based policy, which maximizes the percentage of population vaccinated when the maximum vaccine quantity available is 10 million doses. The corresponding total and shortage costs are shown in Figure 2. As noticed, the vaccine quantities allocated by the model are distributed proportionally to the population of regions. Similarly, the total and shortage costs are higher for regions with larger population.

In contrast, in the age-based policy, we incorporated age-based constraints into the model (constraints 4 and 5) to prioritize the high risk age groups over others. Three different minimum ratios of individuals to be vaccinated at high risk age groups are used, 100%, 90% and 80%, respectively. Table 2 shows the results of age-based policy used to allocate 10 million doses over different age groups. As can be seen, the total number of individuals vaccinated when 100% of population at high risk age groups received vaccine are higher than those vaccinated when vaccinating 90% and 80%, so the shortage cost is lower. However, the total cost is higher when reducing the number of individuals vaccinated at high risk age groups. In this case, more individuals at low risk age groups are vaccinated; which needs three doses per individual compared to two at high risk age groups. Therefore, the total cost is higher and the total individuals vaccinated are fewer when 90% and 80% of population is vaccinated than those when vaccinating the whole population at high risk age groups.

The third allocation policy is a hybrid of age and region-based policies where both age and region-based constraints are incorporated into the model. Consequently, the maximum available quantity of vaccine is allocated based on the population of regions while prioritizing high risk age groups within a region. Figure 3 shows the total number of individuals vaccinated in the seven regions and the optimal allocation of 10 million doses among these regions. The corresponding total and shortage costs are shown in Figure 4. Compared to the results of region-based policy, the number of individuals vaccinated in each region, doses distributed and their respective total cost are lower, while the shortage cost is higher. This is because more individuals at high risk age groups are vaccinated since they have higher priority; which needs only two doses per individual compared to three at low risk age groups.

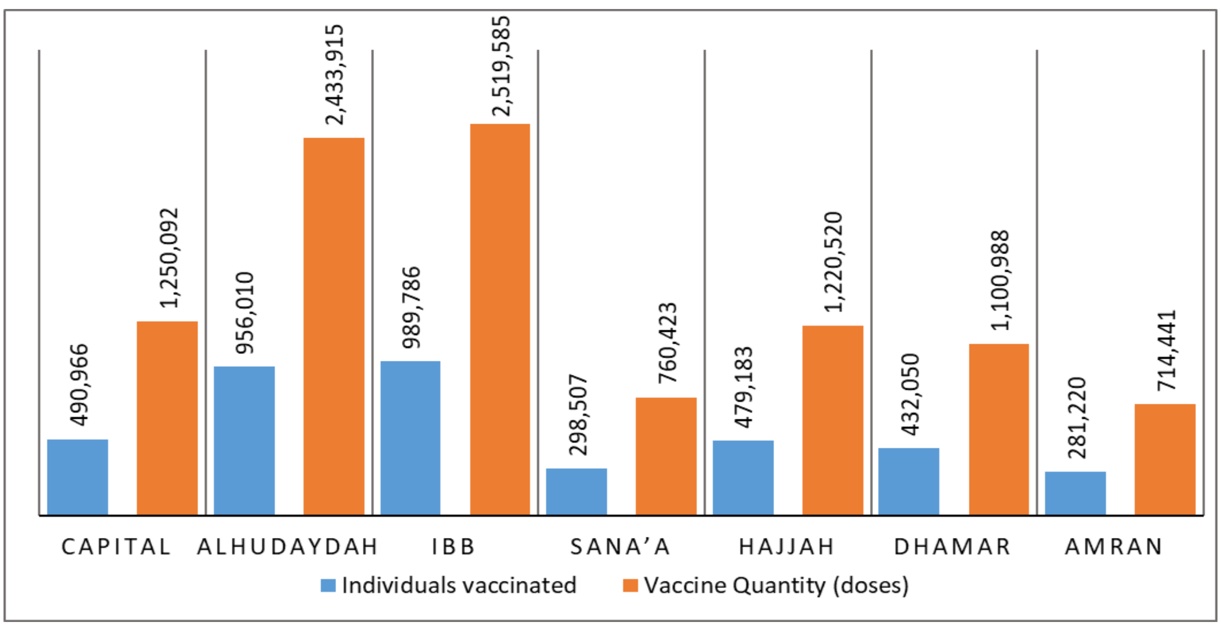

Figure 1: Optimal results for the region-based allocation policy

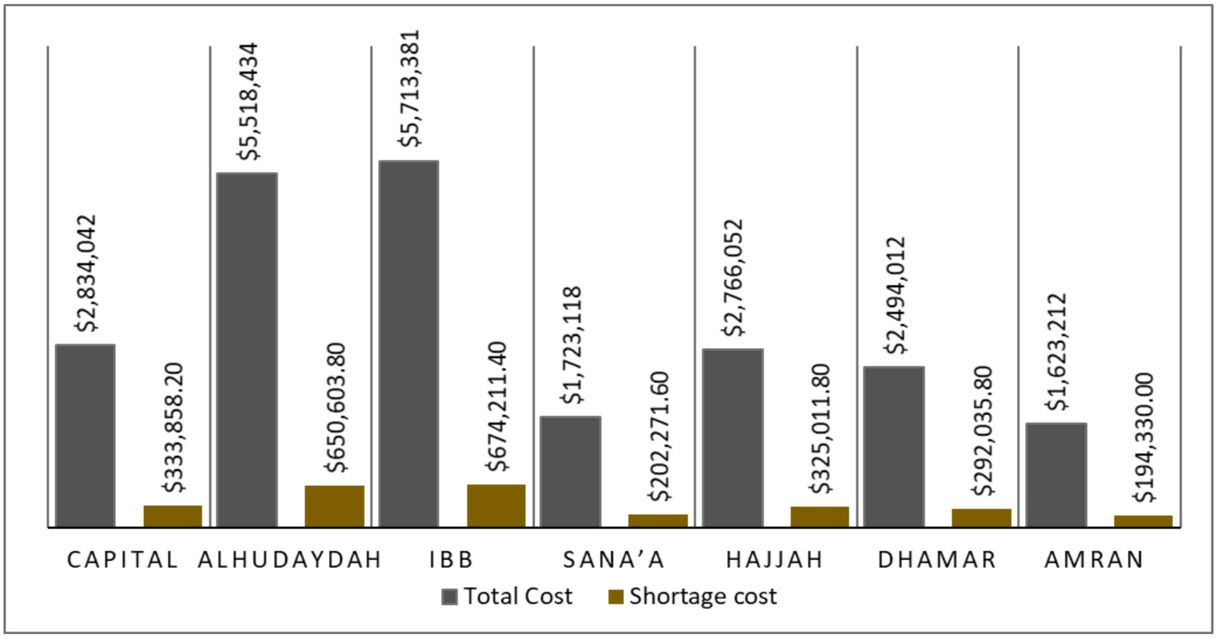

Figure 2: Total and shortage costs for the region-based allocation policy

Table 2: Optimal results for the age-based allocation policy at different values of r_h

Scenario	Individual vaccinated	Total Cost ($)	Shortage cost ($)
$r_h = 100\%$	3,924,611	22,654,206.8	2,672,944.8
$r_h = 90\%$	3,867,538	22,679,815.4	2,684,359.4
$r_h = 80\%$	3,806,549	22,682,721.2	2,696,557.2

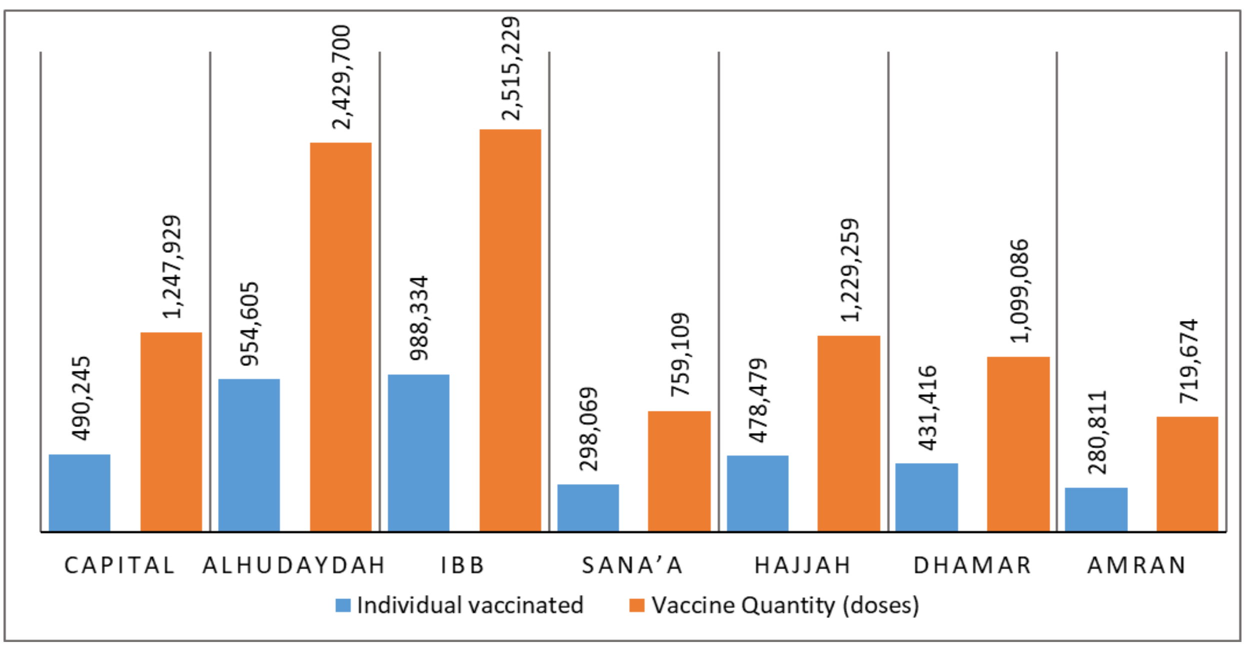

Figure 3: Optimal results for the hybrid allocation policy

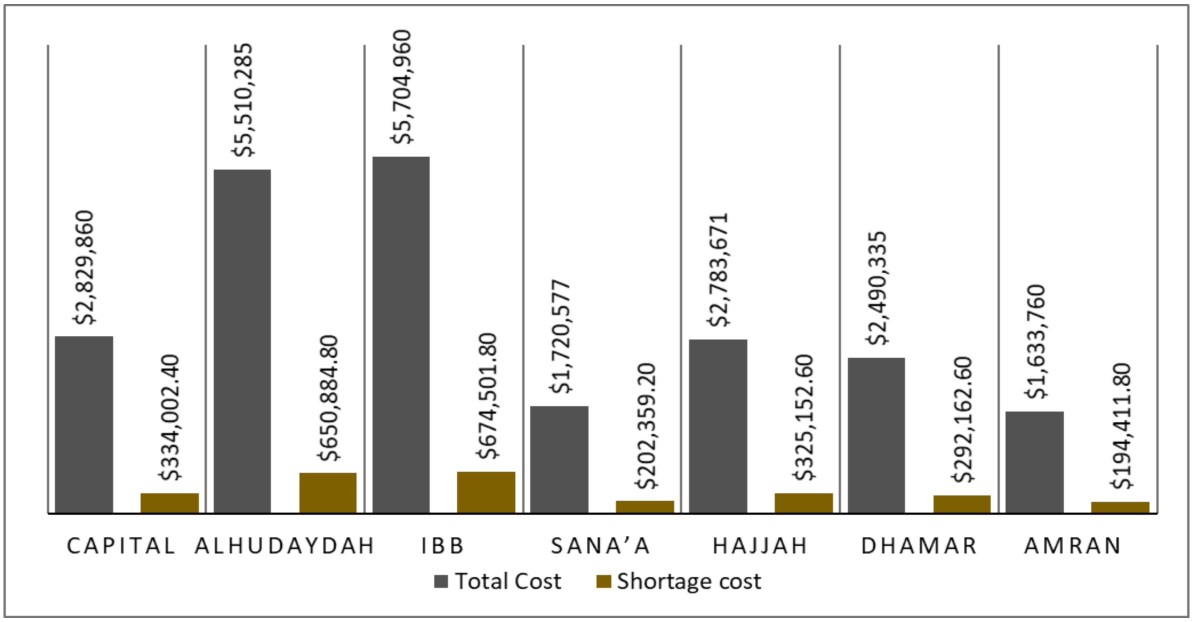

Figure 4: Total and shortage costs for the hybrid allocation policy

Lastly, the three policies are tested to allocate different available quantities of vaccine among the regions and compared in terms of the optimal individuals vaccinated and the total cost. As shown in Table 3, at all various available quantities, the number of individuals vaccinated in both age-based and hybrid policies are more than those vaccinated when region-based policy is used since age-based and hybrid policies prioritize the individuals at high risk age groups which need fewer doses, while the minimum cost is obtained when age-based policy is used. Therefore, the decision makers should trade off between maximizing the population that should be vaccinated and minimizing the cost in order to choose the appropriate vaccine allocation policy.

Table 3: Comparison of age-based, region-based and hybrid policies

Policy	available Doses	Individuals vaccinated	Total cost ($)
Age-based policy	10 million	3,924,611	22,654,206.8
	20 million	7,201,836	41,662,111.8
	40 million	13,923,010	80,644,921
Region-based policy	10 million	3,921,959	22,672,250.6
	20 million	7,240,560	42,005,605.2
	40 million	13,914,720	80,672,256.4
Hybrid policy	10 million	3,927,722	22,673,447.2
	20 million	7,261,059	42,009,719
	40 million	13,927,723	80,674,871

5. Conclusion

In this study, we consider the allocation problem of cholera vaccine quantity among several regions. A mixed integer programming model that helps determine the optimal quantity of the vaccine for various age groups and regions was developed. The model aims to maximize the percentage of individuals receiving vaccination while considering limited doses of vaccine. Three vaccine delivery policies were used to allocate cholera vaccine quantities among several age groups and regions. These policies are compared in terms of the number of individuals got vaccinated and the total cost. It was observed that the number of individuals got vaccinated when age-based and hybrid policies are used are more than those vaccinated when region-based policy is used, while the age-based policy achieved the minimum cost.

To choose among these strategies, the decision makers should trade off between maximizing the population got vaccinated and minimizing the total vaccination cost. As a future work, not only the population and age risk factors but also other factors, such as fatality and incidence rates and the number of individuals that have already been vaccinated should be considered in the model when allocating cholera vaccine. Furthermore, the vaccination budget constraint could be considered in the model.

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