

TOWARD OPTIMAL RESOURCE-ALLOCATION FOR CONTROL OF EPIDEMICS: AN AGENT-BASED-SIMULATION APPROACH

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ABSTRACT

Employing mathematical modeling and analytical optimization techniques, traditional approaches to the resource-allocation (RA) problem for control of epidemics often suffer from unrealistic assumptions, such as linear scaling of costs and benefits, independence of populations, and positing that the epidemic is static over time. Analytical solutions to more realistic models, on the other hand, are often difficult or impossible to derive even for simple cases, which restricts application of such models. We develop an agent-based simulation model of epidemics, and apply response-surface methodology to seek an optimum for the RA output in an iterative procedure. Validation is demonstrated through comparison of the results with the mathematical solution in an RA example for which the analytical solution is known. We apply the proposed approach to a more complicated RA problem in which a number of previous restricting assumptions are relaxed.

1 INTRODUCTION

Epidemics of infectious diseases such as influenza, malaria, and human immunodeficiency virus (HIV) are a major threat for social health. While the World Health Organization (WHO) reports expenditure of more than \$500 million in 2008-2009 to control the spread of epidemics (World Health Organization programme budget 2009), the demand for efficient allocation of these resources is growing. The resource-allocation (RA) problem concerns the best strategy for policy makers to allocate a fixed budget to various populations, through targeted interventions that affect the epidemic's parameters. The efficacy of an intervention on the value of epidemic parameters is usually an increasing function of the cost of intervention and referred as the *cost function* (Brandeau, Zaric and Richter 2003).

Allocation of epidemic-control resources has been studied for many years, and the literature contains analytical models using linear, integer, and dynamic programming (Epstein et al. 2005; Van Zon and Kommer 1999; Earnshaw and Dennett 2003). These models, however, are not applicable to epidemics with non-linear rates of growth and are restricted by several other assumptions like the number of interventions or independence of populations. Recent mathematical approaches to healthcare-resource allocation, on the other hand, suggest advanced models of disease prevalence among several populations, and

consider more general forms of a cost function for prevention programs. Zaric and Brandeau (2001) suggest heuristic algorithms for solving RA problems, and approximating the epidemiological system when closed-form solutions are not known. However, further augmentation in the scope of the problem for real cases could rapidly increase the number and complexity of equations, so the final models might become intractable even for simple instances.

Agent-based simulation (ABS) models are powerful tools that can describe structured epidemiological processes involving human behavior and local interactions. While the computational capacity of ABS models allows for developing large-scale models of epidemics, they are flexible enough to display detailed and complex characteristics of a real system. ABS models have been used to simulate epidemics and assess policy options (Longini et al. 2007; Epstein et al. 2004). Such models represent the system behavior at both macro and micro levels, and allow investigation into system behavior, sensitivity analysis, and predictions.

In this paper, we present an ABS-based approach for allocation of epidemic-control resources. Developing an ABS model of epidemics, we investigate the response surfaces of RA objectives, and apply statistical simulation-optimization techniques to search for the optimal allocation of available resources.

We introduce the RA problem in Section 2. In Section 3 we present the ABS approach, discuss the application of simulation-optimization techniques to address the RA problem, and compare the ABS approach with the analytical approach for a case when the latter is workable, to validate that the ABS approach agrees. In Section 4, we illustrate the efficiency and applicability of the ABS approach through an RA example that is much more complex and cannot be solved by analytical methods. The conclusion is provided in Section 5.

2 PROBLEM STATEMENT

Consider an epidemic of a single disease existing in p populations (e.g. countries, cities, or any other groups of people under study). In order to model the progress of an epidemic within each population, the diversity of individuals in various fields must be reduced to a few key characteristics. This is done by dividing each population into subgroups, also called *compartments*. Each compartment consists of individuals in a specific disease state (e.g. susceptible, infected). Transmission of the disease may occur through one or more diverse pathways, but in this paper we consider only transmission through physical contact with infected individuals. Additional assumptions regarding the epidemic process differ by study.

Disease outbreak is usually far more rapid than the natural vital dynamics of the population (natural births and deaths, migrations, etc.), so that one may neglect them. In this case disease prevalence can be modeled through a set of ordinary differential equations, initially proposed by Anderson and May (1991). In general, however, the timeline of the study may extend to several years due to the nature of the disease, or the horizon of policy making. The epidemic process, in this case, is composed of several aspects of population dynamics, and the associated models incorporate additional epidemic parameters, such as the rate of natural birth/death, rate of migration into and out of populations, etc. These parameters are usually determined by characteristics of the disease and the population under study, and can be defined in stochastic form, or as a function of other parameters.

Resources used for combating a disease are assumed to affect parameters of the epidemic model (e.g. a specific therapy can reduce the disease progression rate) through healthcare interventions. Healthcare interventions target epidemic parameters in a specific compartment or in an entire population. Associated with each intervention is a cost function that depicts the relationship between the amounts invested in the intervention and the values of the associated parameters in the epidemic model. For a total available budget of B , let v_h be the amount of money invested in intervention h , $h = 1, 2, \dots, n$, where $0 \leq v_h \leq B$, and let $\mathbf{v} = (v_1, v_2, \dots, v_n)$ be the investment vector. We define $H(\mathbf{v})$ as the objective function of the RA problem, with investment values of v_h as the decision variables. The general form of the RA problem is

RA : Optimize $H(\mathbf{v})$

$$\begin{aligned} \text{S.t.} : \sum_{h=1}^n v_h &= B \\ v_h &\geq 0 \quad \forall h \end{aligned}$$

The epidemiology literature contains several discussions on the appropriate form of objective functions in health-care policy making (Phillips, Haddix, and Holtgrave 1998). Although the definition and types of objective functions are based on several factors (such as the disease under study, characteristics of the population, and scope of decision making), there are general guidelines in choosing the appropriate function. However, analytical approaches to epidemiological problems are often restricted in form and the number of objective functions, and may become too complex or even intractable for nonlinear or dynamic cases. In a simulation-based approach, on the other hand, models of epidemics provide a virtual reality to generate any desired outputs, and simulation-optimization techniques put no restriction on the form or nature of objective functions. We consider two generally accepted forms of objective functions suggested by Brandeau, Zaric and Richter (2003). The first is to minimize the number of new infections occurring during the time of the study, $INF(\mathbf{v})$, and the second is to maximize the total number of quality-adjusted life years, $QALY(\mathbf{v})$, gained. Let $q_{ij} \in (0, 1)$, $i = 1, 2, \dots, p$; $j = 1, 2, \dots, m$ denote the quality adjustment for life years lived by individuals in compartment j of population i . We assume that quality of life is higher for individuals in the earlier state of disease than for individuals in late states; thus $q_{ij} > q_{i'j'}$ for $j' > j$. For more information on these functions, see Brandeau, Zaric, and Richter (2003).

3 SIMULATION-BASED APPROACH TO HEALTHCARE RESOURCE-ALLOCATION PROBLEMS

In this section we discuss our simulation-based approach to address the healthcare resource-allocation problem. This approach consists of two major steps: creating the ABS model of an epidemic, and applying a simulation-optimization technique to estimate the RA problem. We close this section by investigating the consistency of results with the analytical solution for a relatively simple example where the analytical solution is available, by way of validation of our approach.

3.1 Creating an Agent-Based Simulation Model of an Epidemic

Agent-based modeling and simulation is a relatively new modeling paradigm that has seen extensive application in recent years. While discrete-event simulation (DES) is still more common in operations research, ABS introduces a new way to model complex systems. Such systems are characterized by the fact that their aggregate properties cannot be deduced simply by looking at how each component behaves, since the interaction structure itself is playing a crucial role. In comparison with the top-down modeling approach of DES (where a system is broken into its components represented by blocks, machines, or modules, and entities are defined as passive objects being directed through these components), ABS follows a bottom-up approach. In ABS, a system is modeled as a collection of autonomous decision-making entities called *agents*. Each agent individually assesses its situation, and makes decisions on the basis of a set of rules. Agents interact with one another, and with the environment through a computer code. Over many replications, these interactions can generate large-scale phenomena of interest, in our case the course of epidemics across space and time. This generative nature of such models enables us to focus on the microscopic individual behavior, as well as study the macroscopic pattern of epidemics emerging in a larger scale. In this regard, as Burke et al. (2006) suggest, ABS can provide credible bases for policy analysis when calibrated to actual epidemic data.

We choose NetLogo (2010), a popular agent-based programming language that is particularly designed for modeling complex systems developing over time. Figure 1 shows the proposed ABS logic of an epidemic model implemented as a set of five main sub-procedures: Creation, Contact, Progression, Migration, and Reproduction.

The simulation model is initialized by defining the model global variables and each agent’s attributes. In the create procedure, the epidemic system is created as a collection of agents in p different populations. Each population consists of m compartments with agents in different states of disease, where the initial size (number of agents) of the j^{th} compartment of the i^{th} population is N_{0ij} , $i = 1, 2, \dots, p$; $j = 1, 2, \dots, m$. The contact procedure simulates the process of disease prevalence in each population. Infected individuals in later states of disease can transmit the disease to susceptible individuals (in the first compartment) through random contacts where λ_{ij} is the sufficient contact rate for transmission among individuals of the first and the j^{th} compartment of population i . With progression of the disease at the next procedure, the individuals in the j^{th} state of disease move to the next state with probability θ_{ij} . Migration takes place among individuals in different populations but in the same disease state j , with probability $\phi_{ii'j}$, $i \neq i'$. In the Reproduction procedure, a number of current agents in different populations and disease states die with probability δ_{ij} for each agent. The remaining agents in each population then will have probability of ζ_i to bear new children, who will belong to their parent’s population, but do not inherit the disease. The model is executed until the simulation time reaches the study time horizon of T . The model outputs are defined as $\text{INF}(v)$ and $\text{QALY}(v)$ for individuals in each population. The outputs are reported at the end of each replication.

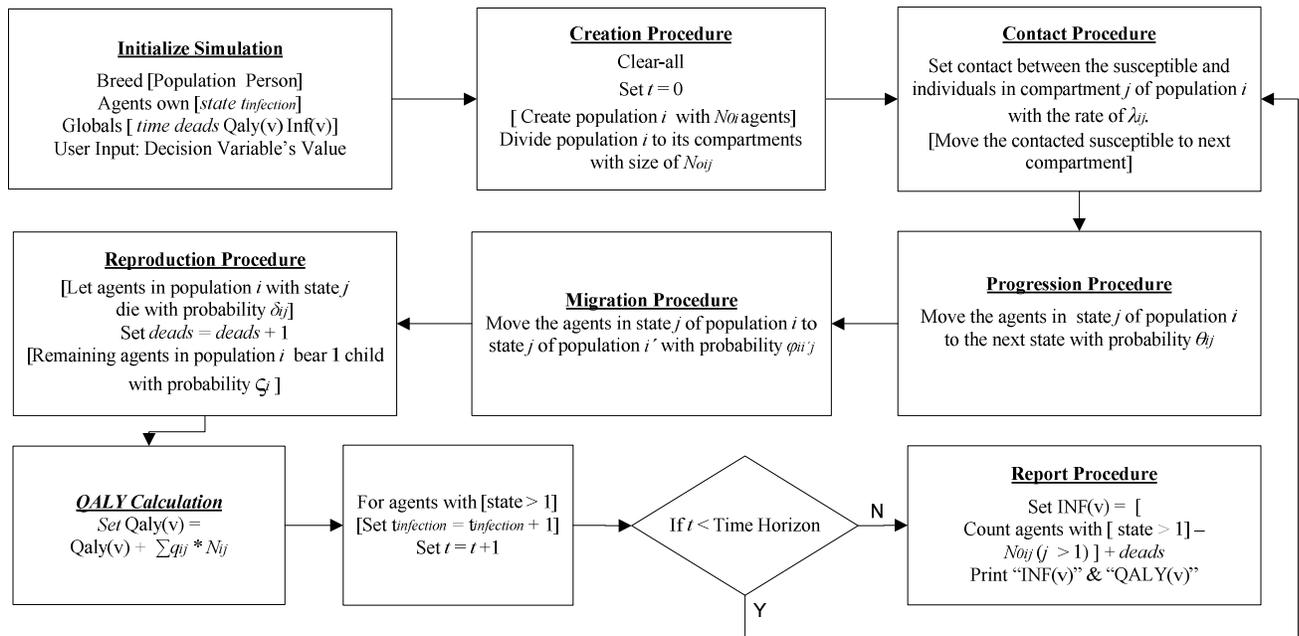


Figure 1: Flowchart of Epidemic Simulation Model

3.2 Applying a Simulation-Optimization Technique to Address the Resource-Allocation Problem

By simulation-optimization we mean a repeated analysis of the simulation model with different values of input parameters, in an attempt to identify the best simulated system performance (Barton and Meckesheimer 2006). However, for the extensive experimentation required for optimization, the simulation models themselves may require excessive computation, so simpler approximations are constructed, often referred to as *meta-models* (Kleijnen 2008) or *surrogate models* (Yesilyurt and Patera 1995). A meta-model, or a model of model, provides a concise representation of the output response and its dependence on accompanying input factors. A meta-model simplifies the simulation-optimization in two ways: the

meta-model responses are deterministic rather than stochastic, and the run times are generally much shorter than the original simulation. However, the meta-model is not an exact replica of the simulation model, so there is a trade-off involved.

Meta-model-based optimization methods use an indirect-gradient optimization strategy to seek the optimal solution. *Response-surface methodology* (RSM) is a collection of mathematical and statistical techniques that are useful for the modeling and analysis of problems in which a response of interest is influenced by several variables and the objective is to optimize this response. RSM is a meta-model-based optimization heuristic that fits first- or second-order polynomial regression models to observed values of Y , the simulation output. An example of a full second-order response surface model would be

$$Y(\theta) = \beta_0 + \sum_{j=1}^q \beta_j \theta_j + 2 \sum_{i=1}^q \sum_{j=1}^{i-1} \beta_{ij} \theta_i \theta_j + \sum_{i=1}^q \beta_{ii} \theta_i^2 + \varepsilon,$$

where ε is an independent normal random variable with mean 0 and variance σ^2 . Initiating from a randomly selected or predetermined local region, RSM designs the appropriate simulation experiment, typically factorial designs for first order, and central composite designs (CCDs) for second order, and fits a local meta-model to the response. This model is then used to decide the direction of improvement called *steepest ascent* (or *descent*). Investigations continue along the steepest direction until no further improvement in simulation output is observed. The procedure then moves to the next iteration by replacing old meta-models with new ones, and improving the result following the steepest direction. The stopping criteria are checked at the end of each search iteration, and the optimal solution is estimated at the end of final iteration. We consider failure to achieve a minimum of 5% improvement in average response as the stopping criterion of our procedure (Castillo 2007).

The RA problem seeks the best strategy to invest a fixed budget among populations through targeted interventions, with the goal of optimizing the problem objective functions. In our model, the simulation outputs, $INF(v)$ and $QALY(v)$, represent the objective functions controlled by the investment vector of $v = (v_1, v_2, \dots, v_n)$. As defined in Section 2, $v_h, h=1, 2, \dots, n$, is the invested amount of money in intervention i , which is designed as the input of the simulation model. In order to solve the RA problem, and to estimate how to optimize the simulation's outputs, we apply RSM to our ABS model in an iterative procedure.

3.3 Comparison of the Simulation-based and the Analytical Approaches

Brandeau, Zaric, and Richter (2003) formulated the problem of resource allocation among non-interacting populations in general, and established conditions that characterized the optimal solution in certain cases. We apply our approach to a numerical example of such a problem, and compare our solution with the results of the exact RA mathematical model, which demonstrates consistency of our simulation-based results and analytical solution.

Assume an epidemic among four non-interacting populations ($p = 4$), with constant sizes of $N_i; i = 1, 2, \dots, 4$ over time. The epidemic within each population is described by a basic susceptible/infected (SI) epidemic model with I_{0i} and S_{0i} denoting the initial proportion of susceptible and infected individuals in population i . The natural rate of birth and death, Δ_i , is the same for both infected and susceptible individuals in each population. The total amount of available funds is B , which can be spent to affect the contact rate among individuals. Therefore, the cost function $c_i(\lambda_i)$ denotes the net present cost of immediately achieving a sufficient contact rate λ_i in population i . The cost functions are assumed to follow non-linear growth over time, independent from each other, and to be strictly decreasing in λ_i , and $c_i(\lambda_{0i}) = 0, i = 1, 2, \dots, 4$; where λ_{0i} is the initial contact rate of individuals in population i at time zero.

Considering the objective function of minimizing the number of new infections, $INF(v)$, we assumed that all epidemic parameter values are continuously uniformly distributed, and applied the simulation-based approach to the RA problem, as discussed above. Subsequently the mathematical model was solved using LINGO (2010), which showed the same results with the solution given by simulation optimization. The results verify the performance of our ABS-RSM approach in this case to represent the epidemic sys-

tem well, and demonstrate the consistency of our proposed approach against the analytical solution of at least this well-known RA problem. However, the precision of the simulation-optimization’s results may still vary due to the random nature of simulation runs, scale of the model, or complex behavior of the response surface in more complicated types of RA problems. This may consequently require further analysis of the response surface to estimate the optimal solution, and statistical hypotheses to test the optimality of the suggested solution. In the following section, we demonstrate the applicability and efficiency of the ABS approach in a more complicated RA problem for which an exact analytical optimum will be extremely hard to derive.

4 ANALYSIS OF A COMPLEX RESOURCE-ALLOCATION PROBLEM

In this section, we apply our approach to a more complicated RA problem in which a number of previous restricting assumptions (e.g. independence of populations\interventions, constant value of epidemics’ parameters over time, equal rates of birth and death, etc.) are relaxed. This example demonstrates how the proposed method can effectively be used in more realistic epidemic models and complex RA problems for which deriving the analytical solution may be impossible. This example was designed with regard to a similar model proposed by Zaric et al. (2001).

Consider an epidemic among $p=2$ populations as in Figure 2. The fixed budget is invested in three different interventions affecting the epidemic parameters. The RA objective is defined as maximizing $QALY(v)$ while maintaining an upper bound for the value of $INF(v)$ at the end of the time horizon. This requirement for the value of $INF(v)$ can eventually barricade the RSM at the boundaries of the feasible region. Luckily for us, such a problem didn’t occur.

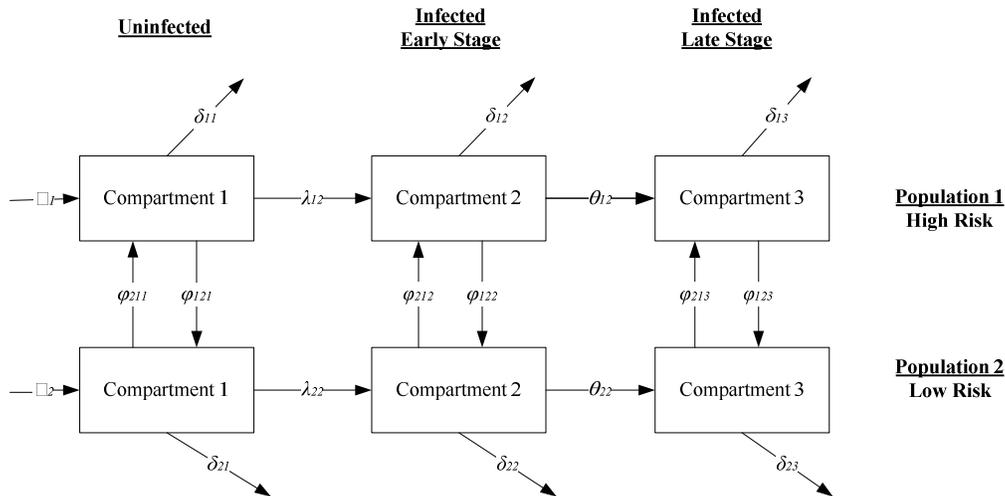


Figure 2: A Three-State Epidemic Model Among Two Interacting Populations

In this example, populations represent high-risk and low-risk groups of people in a society (e.g. the first population may represent intravenous drug users with a higher risk of disease transmission), and migration can take place among individuals in the same compartments of different populations. The epidemiological system consists of three states, i.e. susceptible, early infected, and late infected, with different epidemic parameters. It is also assumed that only the infected individuals in the late state can transmit the disease to uninfected individuals.

Three types of healthcare interventions are designed to control the spread of the disease. Each intervention targets one of the epidemic parameters g_h , $h = 1, 2, 3$, which are assumed to be the migration rate from a high-risk to low-risk group (φ_{121}), and the individual contact rates ($\lambda_{12}, \lambda_{22}$) in each population. Associated with each intervention is a cost function

$$W_{g_h}(v) = M_h(v) W_{g_h}(0) \quad h=1,2,3$$

where $W_{g_h}(v)$ is the future value of epidemic parameter g_h when investing the vector $v = (v_1, v_2, v_3)$ among interventions, $W_{g_h}(0)$ is the initial value of this parameter, and $M_h(v)$ is a nonlinear function of the form

$$M_h(v) = \underbrace{\alpha_h + \beta_h \exp(-\gamma_h \times v_h)}_{P1} + \underbrace{\eta_h \exp\left(-\gamma_{h+1} \left(\frac{v_{h+1}}{a_h}\right)^{b_h}\right)^{-1}}_{P2} \quad h = 1, 2, 3.$$

The first part of this function, $P1$, models the nonlinear effectiveness of each intervention, where α_h is the location parameter taken from a continuous $[0, 1]$ uniform distribution, β_h is a shape parameter with similar values among interventions, and γ_h is a coefficient weighting the amount of investment in each prevention program. Figure 3 demonstrates the nonlinear trend of $P1$ in each intervention for different amounts of investment.

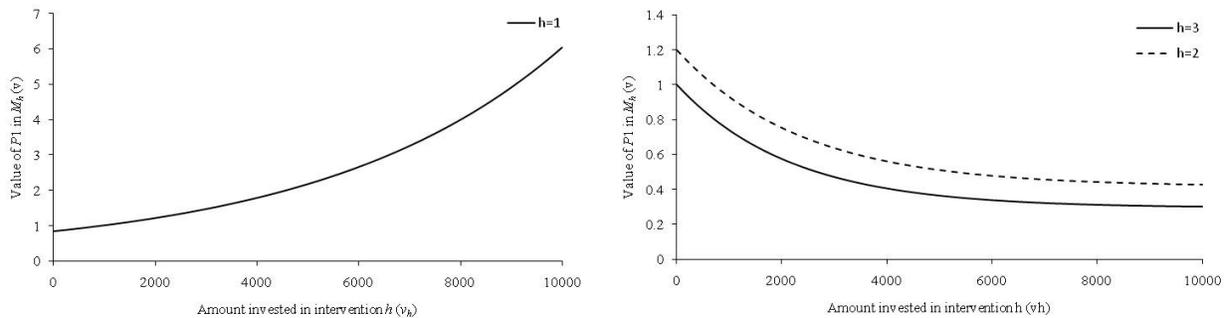


Figure 3: Nonlinear Trend of Intervention h Through the First Part of $M_h(v)$.

Interventions can be thought of as risk-reduction programs in each population. However, the populations are not independent from each other, and the effects of an intervention are not necessarily restricted to the target group. In other words, interactions may occur among interventions, so that the amount invested in one prevention program could influence the effectiveness of another program. For example, consider an epidemic of a viral disease with a higher risk of infection among smokers. A public prevention program is designed to control the rate of disease transmission among the low-risk population. Such a program not only increases the social knowledge about the disease nature and reduces the transmission rate among the low-risk group, but also influences the social norm toward risky behaviors (smoking). This can consequently affect the individuals in the high-risk population to reduce their risky behaviors (quit smoking) and increase the rate of migration from the high-risk group to the low-risk group. This interaction is modeled through the second part of $M_h(v)$ ($P2$) with a nonlinear return to scale. We assume that investment in intervention h ($h = 2$ or 3) can influence the effectiveness of intervention $h - 1$, and consequently improve the value of the parameter g_{h-1} . In this part, the coefficient η_h is taken from a continuous $[0, 1]$ uniform distribution, and the values of a_h and b_h are used to scale the strength of the interaction. The associated values of these cost functions' parameters for each intervention are in Table 1.

Table 1: Associated Values of Cost Functions' Parameters

h	Cost function	$W_g(0)$	α_h	β_h	γ_h	η_h	a_h	b_h
1	$C(\varphi_{121})$	0.112	0.149	0.701	-0.0002128	0.15	100	1.85
2	$C(\lambda_2)$	0.5	0.414	0.786	0.00042126	-0.2	7	1
3	$C(\lambda_1)$	0.7	0.293	0.707	0.00046151	0	-	-

We assume a special type of disease that could reduce the pregnancy chance of infected individuals, and assume that the probability of child bearing is an exponential function of disease duration. Moreover, the disease progression rate of θ_{ij} , $i = 1, 2$; $j = 1, 2, 3$, for each individual is assumed to be a function of disease duration (see Table 2 for formulae and values of parameters), where k is a constant coefficient associated with the severity of disease in each population (early progression of disease is faster in the high-risk population). We also assume exponential death rates of δ_{ij} , $i = 1, 2$; $j = 1, 2, 3$, with different values for individuals in each compartment (Bailey 1975), and define other epidemic parameters as shown in Table 2.

Table 2: Notation and Parameter Values for RA example

Indices		
i, i'	Indices for population $i = 1, 2$	
j, j'	Indices for epidemic model compartments, $j = 1, 2, 3$	
Global Parameters		
B	Total budget	10000
T	Time horizon	20
N_{1j}	Size of compartment j of population 1	500, 300, 200
N_{2j}	Size of compartment j of population 2	1000, 600, 400
Epidemic Parameters		
ζ_i	Entrance rate of population i	$0.25 \exp(-t_{infection} / 10)$
θ_{ij}	Disease progression rate in population i	$1 - \exp(-t_{infection} / k_j)$
k_i	Constant coefficient of disease progression	$k_1 = 4, k_2 = 20$
δ_{1j}	Death rates in compartment j of population 1	$\exp(d_j)$; $d_j = 0.2, 0.23, 0.27$
δ_{2j}	Death rates in compartment j of population 2	$\exp(d_j)$; $d_j = 0.18, 0.21, 0.24$
φ_{211}	Migration rates from population 2 to 1 for in the first compartment	0.4
q_{1j}	Quality adjustment for life years in compartment j of population 1	0.32, 0.17, 0.1
q_{2j}	Quality adjustment for life years in compartment j of population 2	0.55, 0.25, 0.15
Simulation Model Variables		
T	Time of simulation (simulation clock)	
$t_{infection}$	The time of infection	
$deads$	Total number of deaths	

We let $v = (v_1, v_2, v_3)$ be the investment vector, and develop an ABS model of epidemics with the v as the input and the QALY(v) and INF(v) as the outputs reported at the end of each simulation run. The final goal is to determine the inputs that maximize the total value of QALY(v) at the end of time horizon, while maintaining the upper bound of 12500 for the value of INF(v). Considering the binding constraint of the total budget, the RA problem is

RA: Maximize QALY(v)

$$St: \begin{cases} \sum_{h=1}^3 v_h = 10000 \\ v_h \geq 0 \end{cases}$$

Requirement $INF(v) \leq 12500$

The RA problem analysis begins with applying RSM to the simulation model. We start our investigation with the initial vector of $v = (2000, 5000, 3000)$ for the invested amounts in each intervention, and proceed with the investigation in an iterative procedure. A 2^k factorial design is used at the first iteration to obtain a linear meta-model of outputs. The design is augmented with five center points that allow checking the adequacy of the fitted polynomial. The number of simulation replications was 300 during the first iteration; however, this number went up to 1700 replications for the final experiments to obtain a relative precision of 5% for a 95% half-width interval over the point estimation. Investigations were conducted along the direction of maximum improvement in response until no further increase in QALY(v) point estimation was observed. Moreover, the value of $INF(v)$ is checked at each step to assure the requirement of meeting the upper bound. At this stage, the performance of the suggested optimum is checked, and the searching continues in a new iteration if needed. The RSM results are provided in Table 3.

Table 3: Summary of RA Simulation Results

Iteration	1	2	3	4	5	6
Initial point v_1	2000	3003	4080	5180	44478.8	5673.8
v_2	5000	1997	2320	915.3	1352.2	826.2
v_3	3000	5000	3600	3904.7	4200	3500
Region of exploration	500	200	200	200	200	100
Design (CP = center points)	2^2+5 CPs	CCD				
QALY(v)	15,935	16,447	16,572	16,600	16,618	16,800
R^2 (linear meta-model)%	96	46	78	96	64	53

The final approximate optimum is identified through the 6th RSM iteration for an investment vector of $v = (5673.8, 826.2, 3500)$. A CCD experimental design with 5 center points is used to check the performance of the simulation model at this point. We also check the value of $INF(v)$ as the second priority of optimization. Figure 4 shows the overlay contour plot of both responses ($QALY(v) > 16800$ and $INF(v) < 12400$) for this experiment. The black dot in this figure demonstrates the approximate stationary point of $v = (5708.8, 802, 3491)$ with the corresponding value of $QALY(v) = 16800.2$ and $INF(v) = 12188.1$ for the outputs.

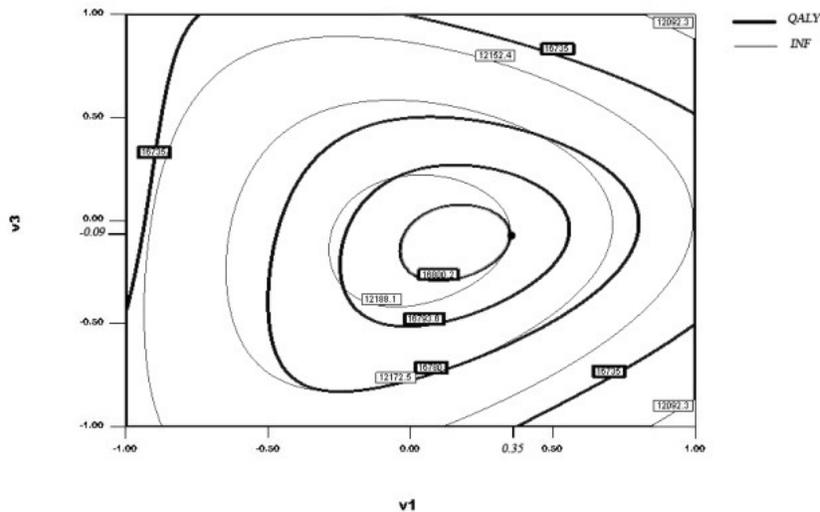


Figure 4: Overlay contour plot of responses

5 CONCLUSION AND FUTURE WORK

This paper presented an agent-based-simulation approach for allocation of epidemic-control resources. The proposed approach considers diverse resource-allocation problems with only general and weak assumptions made about the shape of the cost function and the underlying epidemic structures. Applying optimization-approximation techniques to the ABS model of epidemics, we solved the RA problem in a stepwise procedure. We demonstrated the consistency of our results with an analytical solution through a simplified RA example for which analytical results were previously derived. The application of the suggested approach is finally discussed in a more complex and realistic RA example for which deriving an analytical solution might be impossible.

Use of the ABS approach introduces several advantages to this type of research. Compared to other more-common simulation approaches such as discrete-event simulation where modeling is done at the macroscopic level and entities are just passive objects flowing through block diagrams of the model, ABS allows us to design detailed individual behaviors and their interactions at the microscopic level, so that the developed models will eventually provide a valid representation of population dynamics and disease prevalence through the course of time. The flexibility of the developed model, on the other hand, enables us easily to incorporate new assumptions about populations' characteristics and disease characteristics. We developed our ABS models using the NETLOGO software, which despite the ease of programming, suffers from a lack of statistical or optimization tools' support for analysis of the simulation output.

Future work includes migrating the simulation model of epidemic to other commercial ABS platforms such as REPAST, development of a comprehensive simulation model of epidemics with other means of transmission, extension of our optimization approach to dynamic RA problems, and more robust statistical testing of optimality conditions for the derived solution.

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