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Publication details, including instructions for authors and subscription information:
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To cite this entry: Turgay AyerPinar KeskinocakJulie Swann. Research in Public Health for Efficient, Effective, and Equitable Outcomes. *In* INFORMS TutORials in Operations Research. Published online: 27 Oct 2014; 216-239.
https://doi.org/10.1287/educ.2014.0129

TUTORIALS IN
OPERATIONS RESEARCH
INFORMS 2014

 | ISBN 978-0-9843378-5-9
http://dx.doi.org/10.1287/educ.2014.0129

Research in Public Health for Efficient, Effective, and Equitable Outcomes

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Abstract Public health focuses on preventing disease, prolonging life, and promoting health in a population, and there are many ways in which operations research and management science (OR/MS) researchers can contribute to improved decision making in this area. In this tutorial, we discuss examples of work in several areas of public health, including access and equity, disease screening, chronic diseases, and infectious diseases. In each of these areas, we give a brief overview of challenging issues and related literature, give a specific example of a research topic, and point to potential future directions for research. We describe several trends that could impact future public health research including population ageing and an increased use of electronic records. The tutorial is intended to introduce OR/MS researchers to the many opportunities for having a positive impact on specific populations and society overall, through OR/MS research related to public health.

Keywords operations research; management science; analytics; public health; health systems; access; equity; chronic disease; infectious disease; screening

1. Introduction

Public health has been defined as "the science and art of preventing disease, prolonging life and promoting health through the organized efforts and informed choices of society, organizations, public and private, communities and individuals" Winslow [121, p. 30]. Public health has been around for centuries, with a focus on clean water and sanitation (Romans), quarantining during epidemics (medieval times), and vaccinations (beginning in the 1800s). Public and population health are crucial for the proper functioning of society, since a strong public health system can lead to longer lives with high quality of life. The role of public health may be even more important as populations continue to grow, the gap between income groups in society increases, and technology enables large-scale studies of populations.

As computer capabilities have increased, the health systems in many countries have also seen a rise in the use of electronic health records, which offer great opportunities for operations research and management science (OR/MS). In the United States in particular, there are also many shifts that are coming as a result of new laws, e.g., the Affordable Care Act, that impact financing as well as many other aspects of public health. Hence, there are many opportunities in the public health area where OR/MS and their related disciplines can contribute to improved decision making, including descriptive, predictive, or prescriptive analysis. The rich context of public health problems also promotes interdisciplinary research between OR/MS and other fields, including life sciences, epidemiology, statistics, and economics. In this tutorial we describe several areas where OR/MS research is having an impact on the public health sector.

The public health system is complex, encompassing international organizations, government agencies, insurance companies or managed care organizations, healthcare providers, and patients. Such entities interact in a complex fashion and often have multiple and conflicting

objectives. In this article we focus primarily on public health in the United States, although we point to some public health problems in other settings as well. Examining the offices and centers of the Centers for Disease Control and Prevention (CDC) points to the wide variety of areas in public health that need to be addressed, including infectious diseases, chronic disease prevention and health promotion, health injuries, birth defects, preparedness and response, population surveillance, health laboratories, and health equity.

In some systems one has an objective to achieve, such as minimizing the cost of delivering a set of goods across a network. Broadly speaking, this could be called "efficiency," which is the accomplishment of an outcome with the minimum time, effort, or resources needed. In addition to cost and efficiency, effectiveness and equity are also important in public health. "Effectiveness" refers to whether the best or desired outcomes (which could be measured as lives saved, improvement in quality of life, disease incidents being prevented, etc.) are being achieved through appropriate actions. "Equity" focuses on whether opportunities exist or outcomes are achieved in a fair or equitable fashion across a system (e.g., geographical areas such as urban versus rural, or across population groups with different demographic or socioeconomic characteristics). Equity is much more important in the public health sector than in many other industries and sectors, where achieving the maximum outcome may be the goal. Of course, there are trade-offs between any of these objectives (or others), where increasing equity often may lead to higher costs or results in solutions that have a lower total outcome for the system.

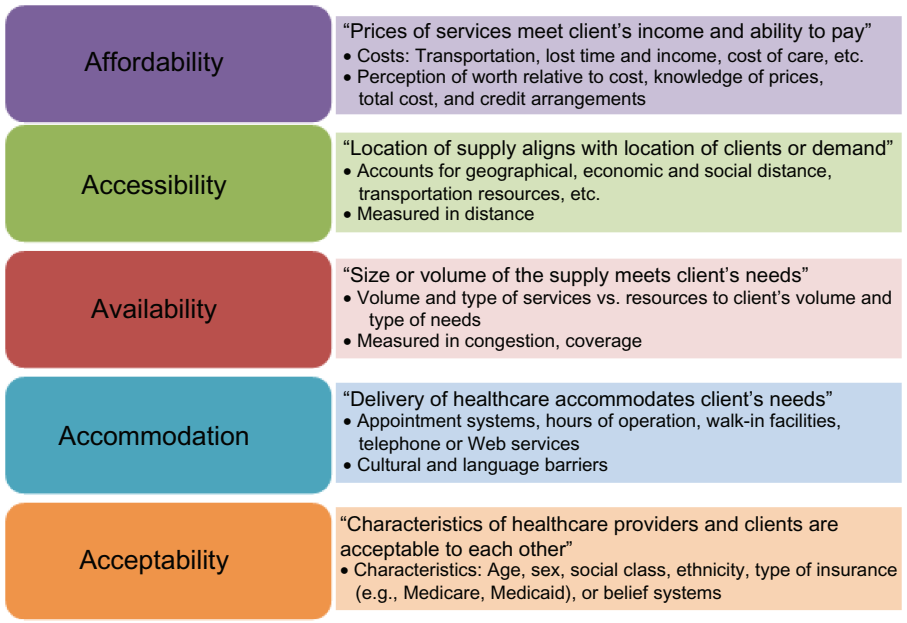
A number of trends are affecting the public health system, and thus the areas of potential research. Infectious diseases continue to be a problem (as they have been throughout time), and the global nature of the world enables them to spread quickly. Many technologies have been created that allow us to screen for diseases in advance, which then begets questions of who, when, or how often to screen. Chronic diseases (e.g., cancers, diabetes, heart diseases) are putting increasing burdens on many societies, where many more individuals worldwide are living with at least one chronic disease. In addition, the rapidly growing elderly population is also a major concern in many countries. For example, people 85 or older constitute the fastest growing segment of the U.S. population and consume most of the country's healthcare resources. This rapidly growing elderly population often suffers from multiple chronic conditions such as hypertension, heart disease, stroke, diabetes, etc., which make screening, treatment, and management of conditions more complex.

In this article we consider a sampling of these areas and point to other trends in the conclusions section below. Specifically, we examine access to healthcare services and equity across a network, screening policies for populations, chronic disease, infectious disease, and global public health problems. In each section, we define the area, point to some of the related research, and give an overview of the research questions and the types of models that can be developed. We focus especially on results that are more recent, while we also recommend that readers consider other sources (Brandeau et al. [11], Cochran et al. [28], Denton et al. [35]) for previous research and other additional relevant topics.

2. Access and Equity

Access to healthcare services is crucial for all components of health, including disease prevention, diagnoses, and treatment, as well as promoting healthy living. Financial access has received much attention recently with the discussion around and passing of the Affordable Care Act, but access in public health is a much broader concept. Figure 1 illustrates five dimensions of access as defined by Penchansky and Thomas [88], where, broadly speaking, access can be thought of as a match or fit between patients and providers. "Affordability" includes elements related to finance and an ability to pay; "accessibility" generally refers to the spatial location of supply and demand over the network; "availability" is related to the level of resources that are available relative to the need; "accommodation" can include

FIGURE 1. Five dimensions of access to services as defined by Penchansky and Thomas [88].



whether the delivery system can meet patient needs, such as in relation to language or hours of operation; and "acceptability" refers to whether characteristics of healthcare providers and clients are acceptable (e.g., language, socioeconomics).

For example, there is a large disparity between access to pediatricians in urban and rural areas in the United States (Randolph and Pathman [94]). The U.S. Department of Health and Human Services identified increasing healthcare accessibility as a key step in mitigating widening disparities of health outcomes in children. Inequities in health access are also associated with higher costs and inconsistency in disease treatments.

Spatial accessibility has a natural link with the OR/MS disciplines, as optimization methods are well suited to study networks of supply and demand. The *measurement* of spatial accessibility is one important topic in public health, since understanding the status quo in access and the associated disparities across a network or across populations can inform efforts to improve the system. Moreover, understanding spatial access is particularly important when there are major shifts in the system, such as when demand increases substantially because of population ageing or changes in financial access.

At a fundamental level, measuring spatial access is related to the services in an area (e.g., physicians) compared to the population in an area. In the literature on measurement of spatial access, researchers often focus on measuring *potential* access, reflecting what access is possible, rather than *realized* access, which can include affordability and other factors. A popular set of methods used in the public health community is based on two-step floating catchment areas (2SFCA) (Luo and Wang [74]), which were motivated by gravity models (Weibull [115]). These methods define catchment zones to measure the population around facilities in the first step and catchment zones capturing facilities around populations in the second step in order to ultimately arrive at a composite measure of spatial access for each population location in the network. An alternative approach is to use optimization to assign patients and providers in the network (Wang [114]), which allows one to estimate travel distance, congestion experienced at a provider, and coverage over a network.

There are a number of advantages of optimization over the catchment methods, as outlined in Li et al. [71]. For example, optimization models can be used to capture the potential experience of a patient, rather than simply reflecting what choices the patient has available.

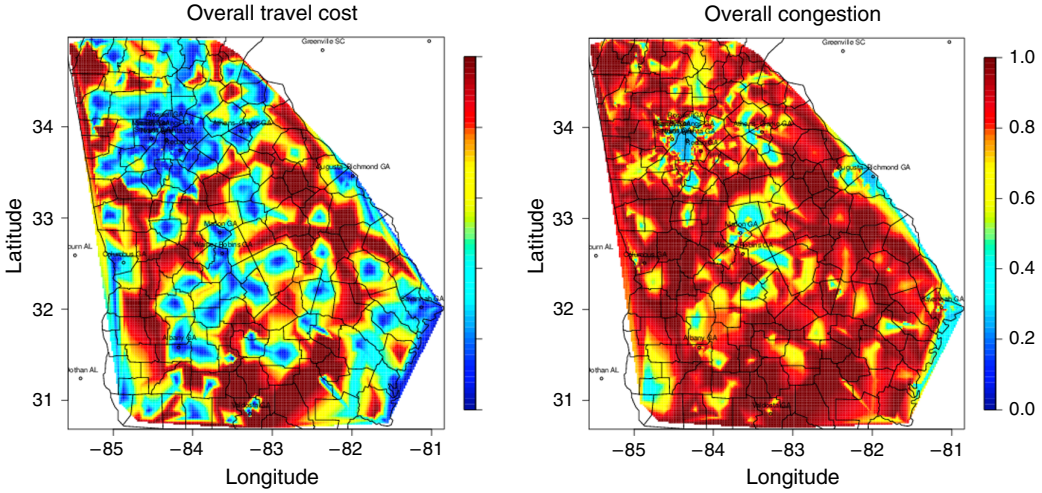
The paper also demonstrates that the 2SFCA methods overcount the demand in the network relative to the size of the population and that the 2SFCA methods do not capture the cascading effects across a system based on congestion.

Serban and Swann have used two kinds of optimization models to measure access in a set of papers (Fitzpatrick et al. [45], Li et al. [71], Nobles et al. [81], Stamm et al. [108]). The first is a centralized optimization model, where there is a perspective of a centralized planner like that commonly found in optimization models. The variables represent which patients are assigned to which providers, and there can be a variety of constraints. Objective functions could include minimizing travel distance if service level is subject to constraint, or many other variations.

Nobles et al. [80] have measured access for children and youths to pediatric services across the state of Georgia, with a special focus on understanding the differences in access between populations under public insurance (Medicaid) versus others in the network. Their model incorporates constraints on patient mobility with different travel distances with or without cars, limitations on physician maximum caseload, limitations on which physicians accept Medicaid patients, and constraints to balance congestion in small areas. Travel distance is minimized subject to meeting a minimum coverage level across the system. Figure 2 shows the estimated distance and congestion for pediatric services in Georgia. Overall, the results include that the population of children on Medicaid had lower levels of access than others in the population. Spatial statistics techniques were used to determine factors that were associated with lower access; a key finding is that higher access was consistently associated with higher income but population density had a nonlinear relationship over the network. The models were also used to test different types of interventions in the system, such as increasing the maximum caseload of patients per physician or increasing the percentage of physicians accepting Medicaid patients. Of the interventions tested, we found that increasing the caseload of Medicaid patients for physicians already accepting Medicaid was more effective than other interventions. More recently, this type of analysis was extended to study access to primary care for children across 14 states (Gentili et al. [49]).

An alternative type of optimization model allows user choice on where to receive service across a network. In these models, patients may trade off different elements in their choice, such as the travel distance to a location versus the availability of providers at that location relative to the population served (this can be called "scarcity" or "congestion"). A weight can be used to adjust the relative preference of distance compared to congestion. The model

FIGURE 2. Distance to (left) and congestion at (right) pediatric care for children in Georgia, as estimated using optimization models presented in Nobles et al. [81].



includes an equilibrium condition for each patient or population, where it is satisfied for the system when no one can unilaterally improve their choice by switching to a different facility. Stamm [107] shows that an equilibrium is guaranteed to exist over the network, describes approaches to solve it, and shows how facility congestion weights can be optimized such that individuals will select the locations that were assigned in the centralized optimization model. In Stamm et al. [108], decentralized models were used to estimate the spatial access to the flu vaccine during the emergency response to the H1N1 pandemic in 2009–2010; and in Li et al. [71], decentralized models were used to estimate spatial access for specialty care for cystic fibrosis over the entire United States.

Another advantage of optimization methods in studying spatial access is that they can be used to design interventions. The classic approach is a facility location model (Daskin and Dean [33]) with a fixed and variable cost to a new facility, and which can incorporate numerous aspects that are specific to the application. For example, Khalid and Scherrer [65] selected where to locate community healthcare clinics over a network to maximize access to primary care services, and Griffin et al. [53] maximized the expected outcomes resulting from new clinic locations. These types of models can also aid in selecting new locations for telemedicine, satellite clinics, or mobile clinics. They can also be used to compare different kinds of interventions, such as the analysis in Griffin et al. [55], which compared increasing spatial accessibility to increasing affordability by raising Medicaid eligibility.

Although an optimization model can aid in the measurement of spatial access, methods such as statistics can aid in determining what factors are related to inequities in access, quantifying the statistical link between spatial access and healthcare outcomes, or showing which interventions result in statistical improvements to the system. Combining the disciplines of statistics and optimization has been a focus of our work in healthcare access. For example, Stamm et al. [108] studied associations, specifically what factors were associated with inequities in access to the flu vaccine during the pandemic (based on a decentralized optimization model) and found that income and minority population was not associated with inequities across most of the southeastern United States. Fitzpatrick et al. [45] connected with outcomes, by using optimization to measure spatial access, then included the measurements in a statistical model to quantify the impact that reduced access has on healthcare outcomes for asthma. The authors found that the link with outcomes varied across states and was the strongest for children in certain age brackets. For other OR/MS work in the area of access or equity, see, for example, Balasubramanian et al. [8], Chan and Green [27], Deo et al. [37], and Woodall et al. [122].

Much work remains to be done in healthcare access and equity. Optimization models will continue to be useful in measuring and improving access over a network, especially as the Affordable Care Act changes the financial access of many populations. It is also of interest to study access over time, or delve further into the different dimensions of access. Finally, as technology advances, this poses both more opportunities for access to services and the risk of increasing the gap between populations that have access and those that do not, so OR/MS researchers are encouraged to consider these aspects of access and equity.

3. Disease Screening

Preventing any disease can be grouped into three levels: primary prevention, secondary prevention, and tertiary prevention (Papadakis et al. [85]). Primary prevention refers to taking precautions to remove or reduce disease risk factors (e.g., immunization, ceasing or not starting smoking). Secondary prevention refers to early detection of diseases in order to reverse or slow the course and improve prognosis (e.g., routine measurement of blood pressure, HPV screening for cervical cancer). Lastly, tertiary prevention refers to minimizing the effects of established disease (e.g., improving lipid profiles in patients with cardiovascular disease). In this section, we focus on secondary prevention via mass screening.

TABLE 1. Estimated new cancer cases and deaths in the United States in 2013 for most common cancers (American College of Surgeons Commission on Cancer [4]).

	Estimated new cases		Estimated deaths	
Cancer type	Male	Female	Male	Female
Lung and bronchus	118,080	110,110	87,260	72,220
Prostate	238,590		29,720	
Breast	2,240	232,340	410	39,620
Colon	50,090	52,390	26,300	24,530
Skin	48,660	34,110	8,560	4,090
Lymphoma	42,670	36,360	11,250	8,950
Leukemia	27,880	20,730	13,660	10,060
Pancreas	22,740	22,480	19,480	18,980
Liver	22,720	7,920	14,890	14,890

Mass screening of asymptomatic individuals can diagnose diseases at most treatable earlier stages (Papadakis et al. [85]). On the other hand, from society's perspective, although a small fraction of the population (i.e., patients who have disease) benefits from screening as a result of early detection and improved survival, the vast majority of the remaining population (i.e., the disease-free population) receives little or no benefit. In addition, in most cases the majority of the population is exposed to harms, such as false-positive test results triggering further unnecessary invasive diagnostic procedures (e.g., biopsy following a false-positive mammogram), complications from the screening procedures resulting in morbidity and mortality (e.g., perforation during a colonoscopy), and overtreatment (i.e., detecting and treating cancers that would not surface in the absence of screening) (Knudsen et al. [66]).

Furthermore, mass screening is a costly investment. For example, the annual cost of mammography screening is estimated to be around $7.8 billion (O'Donoghue et al. [83]). With the rapidly rising healthcare expenditures (currently costing about $2.3 trillion, accounting for 17% of the U.S. gross domestic product), efficient allocation of medical resources, including those allocated for cancer screening, becomes a high priority for payers and policymakers. In the remainder of this section, we focus on mass screening for major cancers.

Over 1.6 million new cancer cases and more than 580,000 cancer deaths occurred in the United States in 2013, making cancer second only to heart disease as the leading cause of death (see Table 1 for the estimated number of new cases for most common cancer types among males and females) (Siegel et al. [102]). The lifetime risk of developing cancer is 38% for women and 44% for men, and lifetime cancer-specific mortality is 20% for women and 23% for men (Howlader et al. [59]). The economic burden of cancer is also substantial. The National Institutes of Health (NIH) estimated the 2008 overall annual costs of cancer care in the United States to be $201.5 billion, of which $77.4 billion accounted for direct medical costs (Yabroff et al. [131]). Furthermore, these costs are expected to increase significantly in the future because of expected population growth, population ageing, improvements in survival, and increasing costs of advanced treatment options.

With rapid advancements in medical technology and drug development, most cancers are now effectively curable if they are detected at the early stages. For example, five-year survival increases from 20% to 92% when breast cancer is detected at Stage II-A instead of Stage IV (American College of Surgeons Commission on Cancer [4]).

The objectives of a national cancer screening program are to detect as many cancers as possible at the early and most treatable stages while at the same time minimizing the exposure of the population to avoidable risks and harms (such as false positives, unnecessary invasive tests, and overtreatment). In addition, ensuring the cost effectiveness of a screening program is also important. Currently, screening is recommended for breast, cervical, colorectal, lung, ovarian, prostate, and skin cancers.

Clearly, as the frequency of screening increases, more cancers will be detected, but at the same time this will also result in more false positives, unnecessary diagnostic tests, possible overtreatment, and increased costs. Capturing these trade-offs and balancing these outcomes require a formal analysis and provide several opportunities and challenges for OR specialists. Several important characteristics of diseases and/or tests need to be taken into account in model development, including disease incidence, prevalence, disease-specific and background mortality, aging effects, and accuracy of the screening tests, as often measured by sensitivity and specificity.

Several simulation-based studies have been conducted to address comparative effectiveness and cost effectiveness of various screening strategies for many cancers, including breast, prostate, colorectal, cervical, and ovarian cancers (Etzioni et al. [42], Goldie et al. [51], Loeve et al. [72, 73], Stout et al. [109], Urban et al. [111]). Simulation models provide flexibility to capture detailed disease progression and screening options. Even so, for several problems the number of screening strategies that need to be tested against is large because of uncertainty in optimal age to initiate and end screening, frequency of screening for different risk groups, and which screening modality to use for different subpopulations. In such cases, the use of a simulation model may be prohibitive because of computational intractability.

When simulation models cannot be used, analytical models (typically, stochastic optimization models) are utilized. In the past, several analytical models have been developed to address various cancer screening problems (Alagoz et al. [1]). Such analytical models provide overall insights about the problem dynamics. However, typically, several limiting assumptions have been made to ensure computational tractability. Some of these assumptions include the following: the specificity of the screening test is 100% (i.e., false-positive rate is 0%) (Kent et al. [64]), the test accuracy is the same for all age groups (Lee and Pierskalla [69], Parmigiani et al. [86]), disease progression is stationary (Özekici and Pliska [84]), noninvasive tumors are not harmful and therefore can be ignored (Baker [7]), the screening interval has to be fixed (i.e., only periodic screenings are allowed) (Preston [90]), the decision maker (i.e., patient and/or physician) has perfect information about disease progression (Yaesoubi and Roberts [132]), and the risk of the cancer is the same for the entire population (Prorok [91]).

Ayer et al. [5] proposed an analytical modeling framework to personalize breast cancer screening strategies based on individual risk factors of women and their prior screening history. The authors formulated a finite-horizon, partially observable Markov decision process (POMDP) model for this problem, which addressed many of the common limitations discussed earlier. In particular, the model incorporated detection through both screening and self-detection, and considered age-specific and unobservable disease progression, as well as age-specific test outcomes. The results showed that the proposed personalized screening schedules outperformed the existing guidelines with respect to the total expected quality-adjusted life years while significantly decreasing the number of mammograms and false positives.

In addition, to our knowledge, all of the prior analytical models assumed 100% patient adherence to recommended cancer screening strategies. However, evidence suggests that adherence rates to cancer screening programs are significantly lower than 100%. For example, fewer than 10% of American women undergo annual mammograms over a period of 10 years (Partin et al. [87]). Therefore, considering imperfect adherence is critical in designing optimal cancer screening strategies. In fact, low adherence rates are identified as the primary reason for suboptimal clinical benefit (Sabaté [97]). Ayer et al. [6] assessed the role of heterogeneity in women's adherence on optimal breast cancer screening policies. Unlike the recent U.S. Preventive Services Task Force guidelines, which recommend biennial screening for women over age 50, the authors found that recommending annual screening is likely to result in higher health outcomes than screening every two years. This is because more than half of the U.S. women do not adhere to screening recommendations, and biennial screening appears to be optimal only for average or low-risk patients, who are highly likely to adhere.

Much work remains to be done in cancer screening. Mathematical models allow capturing several important dynamics in disease screening problems and provide a framework to analyze and answer important policy questions. Carefully calibrating such models using realistic data, conducting extensive numerical analyses, and communicating research findings with policymakers are critical to overcome barriers for their policy implementation. Combining optimization methods with statistical tools to rigorously analyze patients' data and carefully calibrate the mathematical models is a promising research direction in this domain. Combining mathematical modeling with methods from behavioral sciences to consider differences in patients' behaviors is another promising direction in cancer screening research. Finally, tailoring screening strategies based on patients' needs and expectations to improve overall health outcomes and patient satisfaction is the ultimate goal in cancer screening and an important step in the area of personalized medicine.

4. Chronic Diseases

Chronic diseases are long-lasting conditions that are persistent and can generally be controlled but not cured. CDC states that chronic diseases including "heart disease, stroke, cancer, diabetes, and arthritis are among the most common, costly, and preventable health problems in the [United States]" (Centers for Disease Control and Prevention [18]). There are a number of causes of chronic disease that are behavioral, including low levels of physical activity, inadequate nutrition, smoking, and excessive drinking. Chronic illnesses cause about 70% of deaths in the United States (Centers for Disease Control and Prevention [20]) and are the leading cause of mortality worldwide (World Health Organization [128]).

OR/MS researchers have many opportunities to improve efficiency, effectiveness, or equity by focusing on chronic disease. Although screening for disease is one area of active research ("secondary prevention," as described in §3 above), there are many other areas of potential research that relate to chronic disease management. Specific examples include identification of high-risk geographical areas of disease (discussed below), optimizing treatment for cancer (Cao and Lim [13]), managing treatment for diabetic patients (Kurt et al. [68], Mason et al. [76], Shah et al. [98]), evaluating treatment for patients with Alzheimer's (Craft et al. [30]), preventing disease through early interventions, allocating resources between prevention and treatment (Alistar and Brandeau [2]), or allocating capacity for chronic care (Deo et al. [36]). We describe work on two specific chronic diseases below.

One great contributor to chronic disease is obesity (defined by some as having a body mass index above a certain threshold). In the United States, obesity has been increasing, and it is now viewed as one of the most serious public health problems of our century. Comorbidities associated with being overweight or obese include diabetes, asthma, heart problems, and many others. Recently, obesity was considered by Wein et al. [120] and Yang et al. [133], who studied screening policies for childhood obesity.

A different aspect of obesity has been considered by Davila Payan et al. [34]. Public health practitioners were interested in intervening to reduce overweight or obesity prevalence among children and youths. To limit the financial investment required, the organization wanted to prioritize the geographical areas for their interventions. However, estimates did not exist of where the prevalence was the highest across the population. Thus the authors developed statistical approaches to estimate the baseline prevalence of obesity in small areas. This approach builds a logistic regression on data from the National Health and Examination Survey (Centers for Disease Control and Prevention [15]) to find variables that are statistically associated with a child being overweight or obese. Census data were used to generate virtual populations in each small area across a network, and the level of obesity in each area was simulated using the distribution of coefficients from the regression model. The baseline prevalence in each area was calculated, and areas were prioritized to capture the highest number or percentage of overweight or obese children. See Figure 3 for the priority areas in

FIGURE 3. Priority areas that cover 80% of the overweight or obese children in Georgia, as estimated using approaches described in Davila Payan et al. [34].

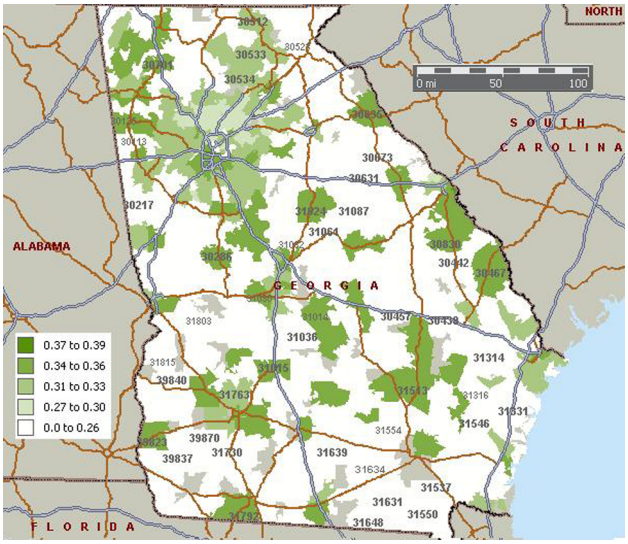
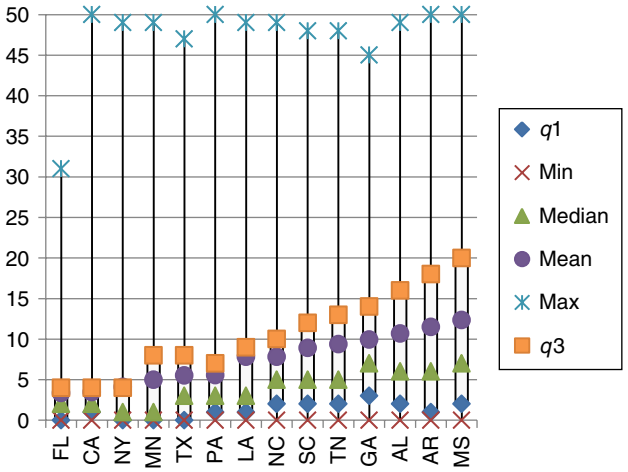


FIGURE 4. Distribution of distance to asthma care (in miles) for populations in each of several states, as estimated using the approaches in Fitzpatrick et al. [45].



Georgia, as estimated in the approach described in Davila Payan et al. [34]. The method was validated by comparing it to school examination data in Arkansas, and we found that it generally performed well. This type of approach to small-area estimation is being explored for a variety of diseases, and we expect the method to continue to be important as more data comes online in health information exchanges.

Another chronic disease that is particularly important among children is asthma. In the United States, approximately 11% of children have asthma, and it is one of the leading causes for visits to emergency departments (EDs) (Centers for Disease Control and Prevention [17]). Fitzpatrick et al. [45] examined the spatial access to asthma care, and, for example, they found that access to asthma care varies greatly across states (see Figure 4, for which optimization models were used to estimate travel distance for each community within a state in order to receive asthma care).

In general, we conclude that chronic disease is understudied in the OR/MS community relative to its importance to the healthcare system and individual patients (although there are many references that we did not include above). We encourage OR/MS researchers to understand some of the most important chronic diseases for adults and children; how they are prevented, diagnosed, or treated; and how systems can be designed to improve outcomes. One area where this may be possible is in utilizing the large amount of healthcare data coming online and using data mining techniques to identify particular patients, providers, or geographical areas. This increasing amount of data will provide opportunities to optimize the treatment or management of individuals' health problems ("personalized medicine").

5. Infectious Diseases

Infectious diseases (also known as transmissible diseases or communicable diseases) are caused by pathogenic microorganisms (e.g., bacteria, viruses, parasites, fungi). Zoonotic diseases are infectious diseases of animals that can cause disease when transmitted to humans (World Health Organization [127]). Infectious diseases can be transmitted from person to person (e.g., influenza, tuberculosis (TB)), can infect a person via bites from insects or animals (e.g., malaria, Lyme disease), or are acquired by ingesting contaminated food or water or other exposures in the environment (e.g., cholera) (World Health Organization [124]). Despite the positive developments in vaccines and treatments, infectious diseases still pose an important threat to human life and have a negative impact on the overall health of the population, as well as the economy. For example, in 2012 there were an estimated 207 million cases of and 627,000 deaths due to malaria (World Health Organization [125]) and 8.6 million TB cases (of which 1.3 million died) (World Health Organization [126]); there are an estimated three–five million cases and 100,000–120,000 deaths due to cholera every year (World Health Organization [124]), and about 34 million people are living with HIV around the world, with an additional 30 million people who have died worldwide since the epidemic began (Centers for Disease Control and Prevention [22]).

Infectious diseases can be *endemic* (i.e., maintained within the population without the need for external inputs), *epidemic* (i.e., numbers of new cases of a certain disease, in a given human population and during a given period, substantially exceed what is expected, based on recent experience (Centers for Disease Control and Prevention [23])), or *pandemic* (i.e., spread through human populations across a large region such as multiple continents, or even worldwide). For example, although malaria is practically nonexistent in Europe and North America, it is presently endemic in a broad band around the equator, in areas of the Americas, in many parts of Asia, and in much of Africa (Roll Back Malaria: The Global Partnership for a Malaria-Free World [95]).

Many infectious diseases can be prevented by vaccines, through environmental measures (such as the availability of clean water and sanitation), or by personal practices (e.g., hand washing, safe sex practices). Infectious diseases can be treated via medication (e.g., antibiotics, antivirals, antifungals, anti-parasitics) or other measures (e.g., around 80% of cholera cases can be treated through oral rehydration salts (ORS)).

According to a recent article published in *Lancet Infectious Diseases*, "There are at least three reasons why operational research is relevant to health. To improve programme outcomes in relation to medical care or prevention, to assess the feasibility of new strategies or interventions in specific settings or populations, and to advocate for policy change" (Zachariah et al. [134, p. 713]). The article also provides a number of examples from the OR/MS literature that have led to policy changes or had other direct impact in practice. Analytical models and decision support tools that aid in the decisions and actions taken in preventing or treating infectious diseases are especially important in resource-constrained environments, such as in developing countries, or in situations (such as pandemics) where a large number of people are affected in many regions in a relatively short period of time. Potential research questions on

infectious diseases, some of which have already been studied in the OR/MS literature, include the following:

- Assessing the effectiveness of infection control measures, such as the use of N95 respirators on the transmission of pandemic influenza (Wein and Atkinson [116]).
- Modeling the spread of anthrax and evaluating interventions such as indoor remediation strategies, vaccines, and antibiotics (Wein and Craft [117], Wein et al. [118, 119]).
- Emergency response and intervention strategies for smallpox eradication or in the case of a smallpox attack (Kaplan and Wein [60, 61], Kaplan et al. [62, 63]).
- Modeling HIV infection transmission and the effectiveness of intervention strategies (e.g., antiretroviral therapy) (Alistar and Brandeau [2], Alistar et al. [3], D'Amato et al. [32], Enns et al. [41], Shechter et al. [99]).

In the remainder of this section, we discuss three examples of how OR/MS tools and techniques can be used for infectious disease control: (i) modeling, intervention strategies, and resource allocation for pandemic planning and response; (ii) catch-up scheduling for vaccinations; and (iii) resource allocation for indoor residual spraying for malaria prevention.

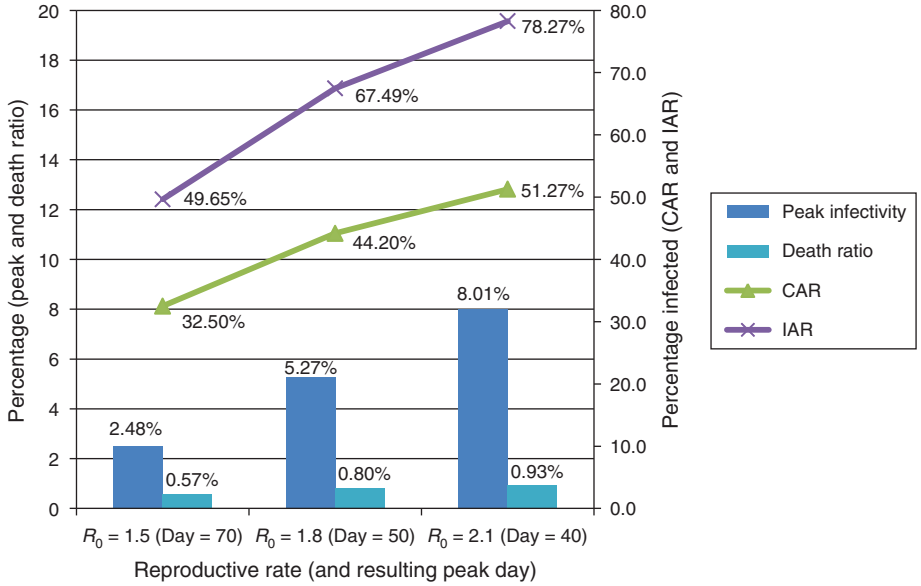
Influenza Pandemic: Disease Modeling, Intervention Strategies, and Resource Allocation

An influenza pandemic (or "pandemic flu") can occur when a new influenza virus emerges; since humans would have little or no immunity to the virus, it can quickly spread worldwide, even healthy people may be at risk for serious complications, it can potentially overwhelm healthcare resources, and it could have a major impact on the public and the economy. In contrast, seasonal flu happens annually, there is often some immunity built up from previous years, and the impact is often manageable (FLU.gov [46]). The 1918 Spanish flu is one of the worst recorded cases of an influenza pandemic in history, whereas the H1N1a pandemic in 2009–2010 was fortunately not as severe. However, the threat of an influenza pandemic continues to exist (for influenza or other zoological viruses) and could result in major outbreaks (Harmon [57]). Researchers in epidemiology and operations research have studied many questions regarding the modeling of an influenza pandemic and the effectiveness of various intervention strategies. More recently, some research has also focused on strategies for allocating scarce resources (such as food and vaccines) during a pandemic response.

There are three common ways to model the spread of an infectious disease in a population: (i) using differential (or difference) equations (Cahill et al. [12], Fraser et al. [47], Grais et al. [52], Rvachev and Longini [96]), (ii) simulation (agent-based) modeling (Ferguson et al. [43], Germann et al. [50], Wu et al. [130]), and (iii) random graphs (Carrat et al. [14]). In general, every individual is assumed to be in one of the disease stages known as susceptible (S), infected (I), or recovered (R) in an S-I-R model. Differential or difference equation models use the cumulative number of people in each stage to define the changes in the system (e.g., disease prevalence) over time. In simulation models, the entire population is modeled by individuals and social contact networks (e.g., households and peer groups). A comprehensive comparison of agent-based and differential equation models is provided by Rahmandad and Sterman [93]. Random graph models construct the contact network and predict the disease spread accordingly. Disease spread models also differ depending on whether they assume homogeneous mixing, where every individual has the same chance to get infected, versus heterogeneous mixing, where the chance of getting infected for an individual depends on the number of his or her contacts.

There are several performance measures commonly used for understanding the spread of the disease and evaluating the effectiveness of intervention policies (Rahmandad and Sterman [93]): (i) *peak infectivity* is the percentage of the infected (symptomatic or hospitalized) population at a given time, (ii) *infection attack rate* (IAR) is the cumulative percentage of people who have been infected (whether symptomatic or asymptomatic) during the course of the disease,

FIGURE 5. Four measures from a simulation of pandemic influenza for the state of Georgia under three values of the reproductive rate.



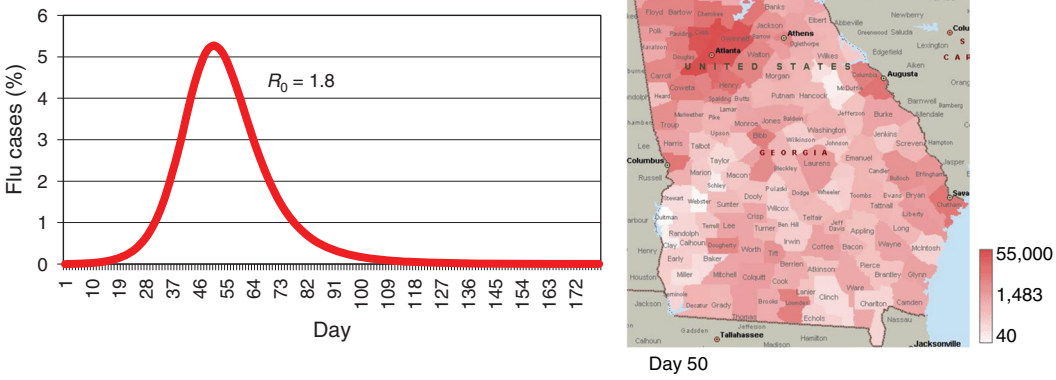
Notes. Peak infectivity and the death ratio are on the left axis, and the clinical attack rate and the infection attack rate match the right axis. Values are summarized from Ekici [38] and Ekici et al. [39].

(iii) *peak day* is the time when the percentage of the infected population is at its maximum, (iv) CAR (*clinical attack rate*) is the cumulative percentage of the people who have been symptomatic, and (v) *death ratio* is the percentage of the people who die because of influenza during the course of the disease. In addition to reducing IAR, CAR, and the death ratio, reducing peak infectivity and delaying the peak day are also desirable. A later peak is desirable for planning purposes, since it provides more time for preparedness efforts—including the potential development and distribution of a vaccine—and a flatter spread (smaller peak) decreases the likelihood of interruption of services and capacity bottlenecks in response activities.

An important parameter used in the modeling of infectious diseases is the basic reproduction number (often denoted by R_0), which denotes the number of cases one case generates on average over the course of its infectious period, in an otherwise uninfected population (Fraser et al. [48]). Figure 5 summarizes the information from Ekici [38] and Ekici et al. [39] on the impact of an influenza pandemic under different R_0 values when there is no intervention. Figure 6 shows the spread of the pandemic over time and space for the state of Georgia from an agent-based simulation.

Several intervention strategies have been studied in the literature, and the analyses focus on the measures discussed above or on cost effectiveness. Research suggests that school or workplace closure and other social distancing measures such as travel restrictions and quarantining can reduce the peak infectivity but might not significantly affect IAR (Ferguson et al. [44], Germann et al. [50], World Health Organization [123]). For example, social distancing measures delayed the spread in the 1918 and 1957 pandemics (Bell et al. [9], World Health Organization [123]) but had little impact on IAR. Recent research suggests that mass gatherings that occur within 10 days before the peak can result in as high as a 10% relative increase in the peak prevalence and IAR, and they may have even worse impacts on local communities and travelers' families. In other words, monitoring, postponing, or cancelling large public gatherings may be warranted close to an epidemic peak but not in earlier or later periods during the epidemic (Shi et al. [101]).

FIGURE 6. (a) Projected percentage of people in Georgia with influenza by day in base case with $R_0 = 1.8$, and (b) projected number of infections (logarithmic scale) on day 50 by county in Georgia.



Several researchers have focused on modeling the allocation of scarce resources (such as food or vaccines), either temporally or geographically (see, for example, Berman et al. [10]; Craft et al. [31]; Kaplan et al. [62, 63]; Kress [67]; Matrajt et al. [77]; Medlock and Galvani [78]; Wallinga et al. [113]). In Lee et al. [70], the authors recommend a policy of vaccinating at-risk individuals first in their simulation study for the greater Washington, DC metropolitan region. Matrajt et al. [77] propose a mathematical model to optimally distribute vaccines in a network of cities, connected by the airline transportation network. They test the performance of pro-rata (i.e., proportional to the population) and children-only pro rata approaches, and notice interesting trade-offs between vaccinating specific geographical locations and vaccinating high-transmission groups. In Medlock and Galvani [78], the results suggest that prioritization of schoolchildren and adults aged 30 to 39 years leads to better outcomes for IAR, death ratio, years of life lost, contingent valuation, and economic costs. Focusing on food distribution, Ekici et al. [39] combined a disease spread model with a facility location and resource allocation network model. Running these models for the state of Georgia, they estimated the number of infections and the number of meals needed in each census tract over time, and they designed a supply chain network. The results show that the impact of voluntary quarantine on food demand and the food distribution network can be significant.

It has been shown that seasonal effects or viral evolution may change the spread pattern of the virus, and lead to multiple peaks (Shi et al. [100]). An interesting research direction would be to link changes in disease spread patterns with the corresponding best intervention strategies or resource allocation decisions. It is also useful to understand how strategies should change for other infectious diseases in the United States or globally, or under different conditions of infectivity or response timeline. Finally, it is important to continue to link the characteristics of infectious diseases with operational aspects of planning and response, including designing a corresponding supply chain.

Catch-up Scheduling for Vaccinations

There are many infectious diseases that are preventable by appropriate administration of vaccines. For example, polio was eliminated from the United States in 1979 after widespread vaccination efforts, and measles was declared eliminated in 2000 (Centers for Disease Control and Prevention [24], The History of Vaccines [110]). However, measles is still prevalent in other parts of the world; in 2011, there were 158,000 measles deaths globally, with more than 95% of measles deaths occurring in low-income countries (World Health Organization [129]).

In the United States, the Advisory Committee on Immunization Practices (ACIP), along with the American Academy of Pediatrics and the American Academy of Family Physicians

(AAFP), annually publishes immunization recommendations for children from birth to six years old (Centers for Disease Control and Prevention [19]). The ACIP also publishes a recommended adult immunization schedule (Centers for Disease Control and Prevention [25]) with the approval of AAFP, the American College of Obstetricians and Gynecologists (ACOG), and the American College of Physicians (ACP). These published schedules contain recommended ages and specific rules regarding the minimum and maximum allowable age that each vaccine dose may be administered, and they include minimum gaps between doses of the same vaccine. The immunization recommendations for adults are dependent on factors such as medical condition, lifestyle, and work environment, in addition to their age and vaccination history. In Canada, the National Advisory Committee on Immunization (NACI) makes recommendations for immunization; however, many provinces maintain recommendations that differ from those given on a national level, as well as those in other provinces. Depending on the disease prevalence and the demographic differences, vaccine recommendations in different countries (or regions), as well as the recommended ages at which certain doses of a vaccine should be administered, can vary. For example, in the United States, children receive the first recommended dose of measles, mumps, and rubella vaccine between 12 and 15 months of age; in Canada, the first dose is recommended at age 12 months, whereas the first dose is recommended to be given at nine months of age in Ethiopia and in most of sub-Saharan Africa.

If an individual misses one or more doses of a recommended vaccine, it is typically a healthcare professional's responsibility to create a catch-up vaccination schedule that is feasible and that maximizes the person's protection against vaccine-preventable diseases. This task is often very challenging and time consuming. A survey of pediatricians and general and family practitioners has indicated that significant knowledge deficits exist among providers required to construct catch-up schedules for children who have missed one or more doses: of six hypothetical scenarios given, the physicians surveyed correctly constructed only 1.83 out of the six on average (Cohen et al. [29]). The construction of inappropriate schedules may prevent some children from being vaccinated in a timely manner. Following the 2000 U.S. National Immunization Survey (NIS), it was reported that of 16,211 children surveyed in the United States, only 9% received all recommended immunizations at the appropriate times, 55% were undervaccinated at two years of age, and 8% of children received an immunization before the minimum age allowed. Coverage rates for individual vaccines reported following the 2007 NIS show minor improvements. The statistics about untimely vaccination of adults mimic those of the children for various reasons including missed vaccination during childhood or changes in factors such as medical condition, work environment, or lifestyle. For example, the tetanus vaccine is recommended for all adults, but only 57.2% of persons aged 18–64 and 44.1% of persons aged 65+ had received the vaccine recently enough for it to be considered still valid (Centers for Disease Control and Prevention [21]).

The catch-up scheduling problem for each targeted age group (children, adolescents, or adults) focuses on determining the best schedule (in terms of coverage) for each individual given their past vaccination history and current age. Doses of a vaccine may not be scheduled unless they may be feasibly administered and are not contraindicated—e.g., if the previous dose is administered at an age that no longer warrants further vaccination. The schedule also needs to satisfy constraints regarding the minimum and maximum age requirements for each dose of each vaccine and the gap between doses of the same vaccine.

Researchers from Georgia Tech have collaborated with CDC to develop several decision support tools for creating catch-up immunization schedules for children through age 6, adolescents aged 7 through 18, and adults. The tools are available for download (Engineer et al. [40], Smalley et al. [103, 104]) or online use (Smalley et al. [106]). There are two types of input to the schedulers: (1) Vaccine-specific requirements are entered into the schedulers in a tabular form. The requirements may change periodically, or new vaccines may be added to the recommended list; in such cases, vaccine-related information may be updated by authorized

persons without needing to modify the core optimization methodology used in generating the schedules. (2) Through an easy-to-use interface, the users can enter input including date of birth, the dates of administration for each dose, and the number of doses of each vaccine that have been administered. The tool then determines the recommended immunization schedule for the child using a dynamic programming (DP) algorithm (Engineer et al. [40]). These schedulers simplify and expedite the tedious process of constructing immunization schedules and eliminate errors (Smalley et al. [105]).

The DP starts with a partial initial schedule (s_0) consisting of doses already administered, and then extends the schedule by a single time period by scheduling combinations of remaining doses, considering all possible schedules that can be created by extending s_0. Schedules that are infeasible or dominated by another schedule are eliminated, and the algorithm continues to extend the schedules one period at a time by repeating the process. Dominance criteria are shown by defining critical doses whose timing in the schedule may prevent a future dose from being administered; in particular, a schedule with the critical doses scheduled earlier is more flexible for choosing dates for future doses, given that the required spacing between two doses of the same vaccine is typically nondecreasing in relation to the age the first dose is given. Using these dominance criteria and given an individual's vaccination history, the DP algorithm can quickly (within seconds) and consistently construct an optimal immunization schedule for remaining doses to be administered.

Although the Catch-Up Immunization Scheduler for Children works under the assumption that all vaccines in the line-up are recommended for each healthy child, the recommended vaccinations for adults and adolescents vary depending on factors such as the individual's lifestyle, medical condition, and work environment. Therefore, in the Catch-Up Immunization Schedulers for Adolescents and Adults, the user enters additional input by answering a series of questions, including whether or not the individual works in healthcare, lives in a nursing home or long-term care facility, or has had a lab test or physician's diagnosis verifying immunity to certain diseases.

Resource Allocation for Indoor Residual Spraying for Malaria Prevention

Malaria is a mosquito-borne disease caused by a parasite. Symptoms include fever, chills, and flu-like illness, and if left untreated, malaria can lead to severe complications and death. In 2010, there were an estimated 219 million cases of malaria worldwide (65% of cases occurred in children younger than 15 years (Murray et al. [79])) and 660,000 people died; more than 90% of these deaths occurred in Africa (Centers for Disease Control and Prevention [26]).

Commonly used prevention and treatment methods for malaria include (i) indoor residual spraying (IRS), (ii) long-lasting insecticide-treated bed nets (LLINs), (iii) insect repellents, and (iv) anti-malarial drugs. Prevention methods focus on reducing the number and rates of infection by controlling the infected mosquitoes, thereby preventing biting and effectively lowering transmission rates. IRS—spraying insecticides on wall and ceiling surfaces in households—has been shown to be an effective method for preventing malaria (Pluess et al. [89]). The insecticide acts as a repellent and kills the mosquitoes upon contact. Depending on the chemical used in the spray, IRS treatments must be repeated periodically (e.g., a spraying of DDT typically lasts for six months). LLINs, which are bed nets that are treated with insecticides, are draped over sleeping areas and provide protection at night (they repel mosquitoes and kill them on contact), when mosquitoes are most active. The effectiveness of LLINs is estimated to be twice that of untreated nets and 70% more as compared with no net (Raghavendra et al. [92]). However, effectiveness of LLINs heavily depends on proper use, which requires education.

Although inexpensive and readily available medications, such as chloroquine, have been commonly used for the treatment of malaria in the past, because of widespread drug resistance, especially in Africa, there is a need nowadays for alternative medications, which are often expensive. The high cost of medication, combined with limited or no access to a medical

facility for a significant portion of the population in the region, makes prevention rather than treatment the focus across much of Africa.

Malaria has been eradicated in most developed countries—for instance, the United States was declared free of malaria as a significant public health problem in 1949 (Centers for Disease Control and Prevention [16]). Hence, the prevention and treatment options discussed above are currently used in the developing world, where the resources are very limited. Successful implementation of intervention programs requires extensive information (e.g., about the demographics, seasonal disease spread patterns) and careful planning and allocation of resources so as to maximize the benefits for the population.

An example of the use of OR/MS tools for malaria prevention and control has been discussed in Griffin et al. [54, 56], where the focus is on resource allocation for IRS. Implementation of an IRS program often happens under a limited budget and time horizon. On the supply side, the implementation requires multiple resources, including trained workers who do the spraying, equipment (tanks, chemicals, masks, etc.), facilities (for storage and distribution), and vehicles (for transporting the workers to various locations to be sprayed). On the demand side, one needs to consider the population size and malaria risk in different locations, and also seasonal changes in malaria risk (see Mapping Malaria Risk in Africa [75] for risk and seasonality models, maps, and data by MARA). Costs include transportation (which depend on the road quality), equipment, facility, and wages. Given a set of potential target areas for IRS, the goal is to dynamically allocate limited resources to geographic locations over time to maximize the "impact" of the implementation. In particular, decisions include where to locate facilities to store equipment and supplies (strategic), which regions to serve from each facility (tactical), and how many trucks/workers to send to each region in each time period (operational) while at the same time considering budget and other constraints. The "impact" can be measured in different ways, e.g., by the total number of malaria cases prevented, or by the "fair" allocation of resources across regions, where the decisions can be significantly different depending on the objective.

Using OR/MS models for solving problems in the developing world provides many opportunities, since even a small improvement in decision making can have a significant impact, given the extremely limited resources and the lives at stake. However, the development and use of OR/MS models also pose many challenges, including the limited availability of data (on population, infrastructure, costs, etc.), choice of an appropriate objective function (which may include robustness), and embedding the developed models into easy-to-use (and low-cost) decision support tools.

6. Conclusions and Future Research

In this article, we have outlined several types of public health research that are being conducted with the set of disciplines represented by OR/MS. The topics covered range across network considerations around measuring and improving access to healthcare and equity across populations, policy considerations such as what screening practices to use for identifying new cases of cancer, simulations of infectious disease spread accompanied by design of response or strategies to reduce new cases, identification of problem areas in the management of chronic diseases such as asthma, and resource allocation for public health problems globally. The methodologies used across these examples include mathematical programming, simulation, dynamic programming, applied probability, and statistics, with many of the applications incorporating more than one type of methodology to answer a particular research question.

In the public health research that we have performed, we have learned that it is essential to bring in the perspective of the clinician or policy decision maker, and extensive collaborations with providers, physicians, and other scientists has been essential. Moreover, we have found that OR/MS specialists can bring many new ideas and models to the table, but that OR/MS

researchers should also be open to learning about the specific domain and considerations of public health stakeholders. For example, goals in determining appropriate policies may be driven by costs, but could also be driven by considerations of health outcomes or even equity across populations or networks. The problems that we have described are primarily applied in nature but we have also discovered that studying problems in the public health sector can lead to new types of models or new approaches for particular problems.

As we outlined above, there are many important public health problems where the OR/MS community can make an impact. Worldwide, infectious diseases are expected to continue to be a major problem, although for some diseases there has been a push to eradicate the disease (e.g., smallpox, polio, Guinea worm). Eradicating a disease can be quite difficult, and OR/MS and analytics can play a role in identifying pockets of disease and designing strategies to treat or prevent the last cases in the world. For example, polio is now endemic in a limited number of countries, but eradicating the last few cases of the disease requires vaccinating a population that is difficult to identify and reach, with associated logistical challenges (Obregón et al. [82]). Chronic diseases are the leading cause of mortality worldwide and account for 60% of all deaths (World Health Organization [128]). Chronic diseases are also related to initiatives to improve health systems, nutrition, and environmental health (all areas covered by the U.S. Agency for International Development (USAID) (USAID [112]), for example). Worldwide, there is also great opportunity for OR/MS specialists to address problems around maternal mortality and child mortality, where there is a range of contributory causes.

There remain many other areas of public health where OR/MS researchers can contribute. One of these is to perform research that addresses current trends related to population changes. For example, the increasing lifespan of the U.S. population implies that it will continue to be plagued with issues around chronic diseases and end-of-life healthcare costs and quality. In fact, as noted earlier, the elderly people constitute the fastest-growing segment of the U.S. population and they often suffer from multiple comorbid conditions. These comorbidities compete against each other and may change the progression of disease, the ability to tolerate screening, diagnostic, and treatment procedures, as well as mortality itself. As a result, the elderly population consumes most of the healthcare resources. Chronic diseases such as diabetes are common throughout the elderly population in the developed world, and the associated comorbidities (such as heart disease, asthma, and others) will need increasing attention from researchers to make good decisions around prevention, diagnosis, and treatment. For Medicare, the public insurance program for individuals over 65 in the United States, it is estimated that 27.4% of costs are spent in the last year of life (Hogan et al. [58]). OR/MS may be able to assist in guiding patients and their families, as well as healthcare providers and other stakeholders, as they determine which procedures are likely to provide increases in life span without decreases in the quality of life. For example, multiobjective optimization could be useful to outline the trade-offs between different decisions for particular conditions.

A second significant trend is the increasing role of information technology (IT) in the U.S. health system. Health IT may play an important role in creating and supporting new care models and payment to achieve the triple aims in healthcare: improve health outcomes, improve patient experience and satisfaction, and reduce costs. With the Health Information Technology and Economic and Clinical Health (HITECH) Act of 2009, the use of health IT has been expanded significantly in the United States in order to achieve "meaningful use." This includes the use of electronic health records (EHRs), Health Information Exchange (HIE) to connect EHRs across providers in a network, and point-of-use technologies that may be installed in common spaces such as retailers, or technologies installed in homes or enabled through mobile infrastructure. These technologies, taken individually or in conjunction, point to "big data"; so "analytics" is essential for the design and improvement of the healthcare systems of the future. EHRs and HIEs may be mined for population information or associations with conditions, or technologies may be analyzed for their potential to improve outcomes or reduce costs. Technologies may also have a role in reducing disparities (e.g., by

increasing telemedicine in medically underserved locations). Optimization may be useful for some research questions, such as when or what telemedicine applications to install, and simulation may also assist in other questions around use of mobile or home technologies. The push toward analytics and increased health information may also make it possible to personalize medicine, not only through advances in understanding the genome and its implications for incidence rate of a disease or treatment success probabilities but also in terms of personalizing policies such as screening based on individual risk factors. It is likely that there are many opportunities for OR/MS to address problems in these areas of research with the right kinds of collaborators and data available.

A third promising area is mobile health (mHealth), which considers the use of mobile communication devices such as mobile phones, tablet computers, PDAs, etc., together with biosensors and/or Internet/social networking, to manage or improve health. Some of the mHealth applications include data collection, real-time vitals measurement and monitoring (e.g., blood pressure measurers, weight scales, pulse oximeters), home-health monitoring, diabetes management, body computing and monitoring, the maintenance of implanted devices such as pacemakers, and improvement of medication adherence. Although so far the computer science community has been more active in mHealth technologies, there are still many research opportunities in this area for the OR/MS community.

In short, the possibilities for OR/MS in public health research are almost endless. One could identify the diseases or conditions contributing the most to any measure—such as cost to the system, loss of life or reduced quality of life, and number of lives affected—and there would be an opportunity for OR/MS researchers to contribute positively. Collaborators can be found in governmental agencies, research institutions, hospitals and other providers, nongovernmental organizations, or even in other disciplines in academia. The time required to learn about a new domain is not insignificant, but the opportunity for benefit to individuals, populations, and the healthcare system is immense.

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