

# Applications of Operations Research to the Prevention, Detection, and Treatment of Disease

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# 1 Introduction

Advances in medical treatment have resulted in a patient population that is more complex, often with multiple diseases, competing risks of complications, and medication conflicts, rendering medical decisions harder because what helps one patient or condition may harm another. The use of Operations Research (OR) methods for the study of healthcare has a long history. Furthermore, there is a recent and growing literature on emerging applications in this area. This chapter provides examples of contributions of OR methods, including mathematical programming, dynamic programming, and simulation, to the prevention, detection, and treatment of diseases. More extensive surveys of OR studies of health care delivery, including medical decision making, can be found in Pierskalla and Brailer (1994) and Brandeau et al. (2004).

Advances in medical treatment in recent decades have extended the average lifespan of individuals, and transformed many diseases from life threatening in the near term to chronic conditions in need of long-term management. Many new applications of OR are emerging as treatment options and population health evolve over time. For example, in recent years new treatments have become available for various forms of cancer, HIV, and heart disease. In some cases patients are living decades with diseases that previously had low short-term survival rates. As a result, more patients are living with co-morbid conditions, and competing risks, creating challenging decisions that must balance the downside of treatment (e.g. medication side effects, long-term complications) with the benefits of treatment (e.g. longer life expectancy, better quality of life).

Diabetes is a good example of a chronic disease for which medical treatment is complex. With nearly 8% of the US population estimated to have diabetes, it is recognized as a leading cause of mortality and morbidity. It is associated with long-term complications that affect almost every part of the body, including coronary heart disease (CHD), stroke, blindness, kidney failure, and neurological disorders. For many patients diabetes might be prevented through improved diet and exercise. However, due to the slow development of symptoms in many patients, diabetes can go undetected for years. For patients that are diagnosed with diabetes, risk models exist to predict the probability of complications, but alone these models do not provide optimal treatment decisions. Rather, they provide raw data that can be used in OR models to make optimal treatment decisions. This general situation is true of many chronic diseases. As a result there are many emerging

opportunities for applications of OR to disease prevention, detection, and management.

The remainder of this chapter is organized as follows. Section 2 describes important contributions of OR to disease prevention including vaccination and screening methods for detecting disease in a population of potentially infected people. Section 3 focuses on applications to long term management of chronic diseases including selection among multiple treatment choices, and decisions about timing and dosage of treatment. Section 4 reviews some emerging applications to real-time decision making at the point of care and patient decision aids. Finally, Section 5 points out opportunities for future research.

## **2 Disease Prevention and Screening**

Prevention and screening are important factors in determining overall population health. OR has been applied to help inform decisions related to prevention and screening for decades. Two major topics in this area, that are prominent in the OR literature, are vaccination and disease screening. Vaccination emphasizes the prevention of infectious diseases, while disease screening is common for both non-infectious and infectious diseases. Each of these topics will be discussed in detail in this section.

### **2.1 Vaccination**

The biological and genetic sciences have greatly increased the knowledge of how viruses and bacteria operate within the body to create disease. This has led to the discovery of many new vaccines. However the myriad interactions as well as controversy about their effects on individuals, and an overall population, have drawn considerable public attention in recent years. These interactions and effects present several challenges in the utilization of the vaccines for disease control. First, there are a large number of diseases for which effective vaccines are available. Some have specific requirements, such as multiple doses that must be administered within a minimum or maximum time window. Also, some have conflicts with other vaccines. Second, many new vaccines are coming on the market, including combination (multi-valent) vaccines that can cover multiple diseases. Third, for some diseases there is uncertainty about the future evolution of epidemic strains, leading to questions about optimal design of vaccines. Finally, there are challenges in the vaccine manufacturing process

including uncertain yields, quality control, supply chain logistics, and the optimal storage location of vaccine supplies. OR models have been applied to address many of these challenges.

### **2.1.1 Pediatric Vaccination**

Pediatric or childhood vaccination is the most common means of mass vaccination. OR researchers have developed models to aid in the selection of a vaccine formulary, pricing of vaccines, and design of vaccination schedules. Jacobson et al. (1999) proposed integer programming models to determine the price of combination vaccines for childhood immunization. Their models consider all available vaccine products at their market prices and constraints based on the US national recommended childhood immunization schedule. Their objective is to find the vaccine formularies with the lowest overall cost from the patient, provider and societal perspectives. Their integer programming models consider the first five years of the recommended childhood immunization schedule against six diseases. They use binary decision variables to denote whether a vaccine is scheduled for a particular month's visit.

In a later study Jacobson et al. (2006) investigated a pediatric vaccine supply shortage problem to assess the impact of pediatric vaccine stockpile levels on vaccination coverage rates of the current guideline during supply interruption. Their model is similar to inventory models that consider stock-outs as well as lot sizing problems with machine breakdowns. Objectives of their model include optimizing service level, and minimizing a standard loss function. Using their model they concluded the current guidelines are only sufficient to mitigate a vaccine production interruption of eight months.

Hall et al. (2008) considered a childhood vaccination formulary problem that allows for combination vaccines. They proposed an integer programming model to minimize the cost of fully immunizing a child under the constraints of a recommended schedule. They prove their proposed model is NP-hard. They proposed exact algorithms using dynamic programming, and heuristics for approximating near optimal solutions to their model. Engineer et al. (2009) further investigate an extension that involves catch-up scheduling for childhood vaccination. They provide details of a successful implementation of their model as a decision support system.

### 2.1.2 Flu Vaccination

Some diseases evolve rapidly over time, necessitating frequent vaccination on a regular basis. For example, the composition of seasonal flu vaccine changes every year. Wu et al. (2005) proposed a model for flu vaccine design. They used a continuous-state discrete-time dynamic programming model to find the optimal vaccine-strain selection policy. In their dynamic program, the state is represented by the antigenic history, including previous vaccine and epidemic strains. The decision variable (action) is the vaccine strain to be selected, and the reward is the cross-reactivity representing the efficacy of the vaccine. The objective is to maximize the expected discounted reward. Approximate solutions are obtained by state-space aggregation and compared to an easy-to-implement myopic policy based on approximating the multi-stage problem by a series of single period problems. They compare policies suggested by their model to the World Health Organization (WHO) recommended policy. Based on their results, the authors suggest that the WHO policy is reasonably effective and should be continued.

### 2.1.3 Vaccination for Bio-defense

OR researchers have contributed to problems related to vaccination strategy for bio-defense. For instance, Kaplan et al. (2003) analyzed bio-terror response logistics using smallpox as an example. The authors propose a trace vaccination model using a system of ordinary differential equations (ODEs) incorporating scarce vaccination resources and queueing of people for vaccination. An approximate analysis of the ODE yields closed-form estimates of numbers of deaths and maximum queue length. They also obtain approximate closed-form expressions for the total number of deaths under mass vaccination. Using these results, approximate thresholds for controlling an epidemic are derived.

Kress (2006) also considered the problem of optimizing vaccination strategy in response to potential bio-terror events. The author developed a flexible, large-scale analytic model with discrete-time decisions. The author uses a set of difference equations to describe the transition of the number of people at each epidemic stage. The author proposes a vaccination policy, which is a mixture of mass and trace vaccination policies.

#### **2.1.4 Other Vaccination Related Problems**

Several other vaccine-related problems have been investigated by OR researchers. For example, vaccine allocation problems must consider criteria and constraints related to vaccine manufacturing and supply chain logistics. Becker and Starczak (1997) formulated the optimal allocation of vaccine as a linear programming problem. Their objective was to prevent epidemics with the minimum required vaccine coverage. Their linear programming model considers heterogeneity among individuals and minimizes the initial reproduction number for a given vaccination coverage. The optimal vaccine allocation strategy suggests more individuals need to be vaccinated in larger households.

### **2.2 Disease Screening**

Disease screening is important in extending life expectancy, improving people's quality of life. Effective screening can also reduce costs to the health system by avoiding the high costs associated with treatment of late stage disease. However, when and how to screen for a specific disease is a complex decision. For instance, model formulation is often difficult due to unclear pathology and risk factors, uncertainty in disease staging and the relationship to symptoms and test results, and the trade-off between the benefit of early detection and the side effects and costs of screening and treatment. The types of OR methods employed depend on whether the disease is non-infectious or infectious. Following are several examples from each category of disease.

#### **2.2.1 Non-Infectious Disease Screening**

Modeling disease progression among different stages throughout a patient's lifetime, as well as the trade-off between pros (e.g. longer life expectancy, better quality of life) and cons (e.g. side effects and costs of over-diagnosis and over-treatment) of disease screening are central to non-infectious diseases. Shwartz (1978) proposed one of the first models for breast cancer screening to evaluate and compare alternative screening strategies. Their stochastic model consisted of a discrete set of breast cancer disease states and criteria considered included life expectancy and the probability of diagnosis. A significant amount of research on breast cancer screening has developed in recent years (see Mandelblatt et al. (2009) for a review of breast cancer screening models).

Eddy (1983) presented a general model of monitoring patients with repeated and imperfect medical tests. The model considered clinical and economic outcomes such as the probability of detecting a disease, the method and timing of detection, the stage at which the disease is detected, costs, and the benefit of screening based on the willingness to pay. The model incorporates disease incidence, the natural history of disease progression, the effectiveness of tests and subsequent treatments, and the order and frequency of tests. The model is illustrated using a hypothetical example. The model has subsequently been applied in clinical practice to several cancer screening problems.

In order to capture uncertainty in identifying disease states, OR techniques such as partially observable Markov decision process (POMDP) have been applied. For example, Zhang et al. (2010) developed a POMDP model for prostate cancer screening. Due to the slow growing nature of prostate cancer, the imperfect nature of diagnostic tests, and the quality of life impact of treatment, whether and when to refer a patient for biopsy is controversial. The objective of their model is to maximize the quality adjusted life expectancy and minimize the costs of screening and treatments. They assume cancer states are not directly observable but the probability a patient has cancer is estimated from their PSA test history. A control-limit type policy of biopsy referral and the existence of stopping time of prostate cancer screening are proven. The authors compare policies suggested by their model, to commonly recommended screening policies, and conclude there may be substantial benefits from using prostate cancer risk to make screening decisions.

Screening for disease is greatly influenced by the diagnostic accuracy of the tests. An example of work done in this area is given by Rubin et al. (2004) in which the authors use a Bayesian network to assist mammography interpretation. Interpreting mammographic images and making correct diagnoses are challenging even to experienced radiologists. False-negative interpretations can cause delay in cancer treatment and lead to higher morbidity and mortality. False positives, on the other hand, result in unnecessary biopsy causing anxiety and increased medical costs. The American College of Radiology developed BI-RADS which is a lexicon of mammogram findings and the distinctions that describe them. The authors show that their Bayesian network model may help to reduce variability and improve overall interpretive performance in mammography.

Many other diagnostic areas have been addressed over the past few decades including gastrointestinal diseases, neurological diseases, and others.

### 2.2.2 Infectious Disease Screening

In infectious diseases screening, one of the goals is to prevent an epidemic outbreak. Therefore disease progression and communication throughout a population is an important consideration. Lee and Pierskalla (1988) proposed a math programming model for contagious diseases with little or no latent periods. The objective of their model is to minimize the average number of infected people in the population. They converted their model to a knapsack problem. They consider both perfect and imperfect reliability of tests and they show the optimal screening policy has equally spaced screening intervals when the tests have perfect reliability.

Disease screening problems often involve multiple criteria, stemming from the patient, provider, and societal perspectives. For example, Brandeau et al. (1993) provided a cost benefit analysis of HIV screening for women of childbearing age based on a dynamic compartmental model incorporating disease transmission and progression over time. The model is formulated as a set of simultaneous nonlinear differential equations. The authors find the primary benefit of screening is to prevent the infection of their adult contacts. They found that screening of the medium to high risk groups may be cost-beneficial, but it is not likely to be cost-beneficial for low risk women.

Blood screening tests have been used to improve the quality of the blood supply. An early example to improve the performance of testing strategies in the 1980s was done by Schwartz et al. (1990) for screening blood for the HIV antibody, and making decisions affecting blood donor acceptance. At the time the work was done, limited knowledge was available about the biology, epidemiology and early blood manifestations of HIV. Furthermore, the initial and conditional sensitivities and specificities of enzyme immunoassays and Western blot tests had wide ranges of errors. A decision tree, with the decisions probabilistically based on which screening test to use, and in what sequence, was used to minimize the number of HIV infected units of blood and blood products entering the nation's blood supply subject to a budget constraint. The model was used at a meeting of an expert panel of the US National Heart Lung and Blood Institute to inform the panelists who were deciding which blood screening protocol to recommend. The model provided outputs including: expected number of infected units entering the blood supply per unit time, expected number of uninfected units discarded per unit time, expected number of uninfected donors falsely notified, and the incremental cost among screening regimens.

Efficiency of screening can be a defining factor in the success or failure of proposed screening methods. Wein and Zenios (1996) proposed models for pooled testing of blood products for HIV screening. Optimization of pooled testing involves decisions such as transfusion, discarding of samples in the pool, and division of the pool into sub-pools. Several models are proposed to minimize the expected costs. The outcome of an HIV test is measured by an optical density (OD) reading, a continuous measurement which is determined by the concentration of the antibodies. The states of the system are the previous history of the OD readings. A dynamic programming model with a discretized state space and a heuristic solution algorithm are introduced to obtain near optimal solutions. The policy obtained by the heuristic algorithm is proposed as a cost-effective, accurate and relatively simple alternative to the current implemented HIV screening policies.

### **3 Treatment Choices**

The following section focuses on treatment decisions for patients with chronic diseases such as diabetes, HIV, cancer, and end-stage renal disease. Treatment of patients with chronic diseases is often complex due to the long-term nature of the illness and the future uncertainty in patient health. Complicating matters, these patients may have other comorbidities that need to be taken into account when treatment decisions are made. In the following section, two areas related to choice of treatment are presented where OR is used to address challenges related to drug treatment decisions and organ transplantation for patients with chronic conditions.

#### **3.1 Drug Treatment Decisions**

Many diseases involve complex drug treatment decisions, particularly for chronic conditions. Decisions about which medications to initiate, when to initiate treatment, and the appropriate dosage are of primary importance. To complicate matters, often there is uncertainty about the future health of the patient, adherence to treatment, and the efficacy of drugs for a particular patient. Treatment decisions must also take into account the often irreversible nature of treatment decisions. Many treatment optimization models employ the use of a natural history model of the disease and all-cause mortality, incorporating the influence of competing risks into the treatment decision.

### 3.1.1 Choice of Treatment

When there are multiple candidate treatments available, the choice of treatment may be unclear. OR techniques have been used to select treatments. For example, Pignone et al. (2006) present a Markov model to select among aspirin, statins, and combination treatment, for the prevention of coronary heart disease (CHD). The model was used to simulate the progression of middle-aged males with no history of CHD. The model was used to estimate cost per quality-adjusted life year (QALY) gained. The authors found that aspirin dominates no treatment when a patient's ten year risk of CHD is at least 7.5%. If a patient's risk is greater than 10%, combination treatment is recommended.

Hazen (2004) used dynamic influence diagrams to analyze a chain of decisions as to whether or not a patient should proceed to total hip replacement surgery or not. The objective in making this decision was to calculate the optimal expected costs and QALYs under each choice. The use of QALYs for the objective was important because an older person undergoing hip replacement may not have more expected years of life relative to not doing surgery, but the quality of life improvement can be considerable and, quite possibly, worth the cost.

### 3.1.2 Timing of Treatment

With chronic conditions that can span many years, the optimal time to initiate particular treatments may be unknown. There are several studies in the literature researching the optimal timing of treatment. Two models relate to the optimal timing of HIV treatment. This question is of particular interest since patients that begin HIV treatment will only be able to use the drug for a limited amount of time, as the virus builds up resistance to the drug. Shechter et al. (2008) use a Markov decision process (MDP) model to find the optimal time to initiate HIV therapy while maximizing the patient's quality of life. At monthly decision epochs, the decision is made to initiate therapy or wait until the next month to decide. The health states are based on CD4 count and the reward is expected remaining lifetime in months. They assume a stationary infinite horizon model and prove that if it is optimal to initiate treatment at a given CD4 count, it is also optimal to initiate treatment for patients with higher CD4 counts. The model supports earlier treatment, despite trends toward later treatment. Braithwaite et al. (2008) analyze the timing of initiation based

on CD4 counts for varying viral loads. They use a simulation to compare different CD4 count thresholds for initiation of therapy. The model compares expected life years and QALYs for the different strategies of initiation. In agreement with Shechter et al.'s finding, the simulation suggests that the use of earlier initiation of treatment (higher CD4 count thresholds) results in greater life years and QALYs.

Agur et al. (2006) develop a method to create treatment schedules for chemotherapy patients using local search heuristics. The model simulates cell growth over time and finds two categories of drug protocols: one-time intensive treatment and a series of nonintensive treatments. Chemotherapy schedules are evaluated based on a patient's state at the end of a given time period, number of cancer and host cells, and the time to cure. Simulated annealing, threshold acceptance, and old bachelor acceptance are used to obtain better treatment schedules. The authors report good results with all three techniques, but they show simulated annealing resulted in the greatest computational effort.

Denton et al. (2009) investigated the optimal timing of statin therapy for patients with type 2 diabetes. This problem is formulated as a discrete time, finite horizon, discounted MDP in which patients transition through health states corresponding to varying risks of future complications, their history of complications, and death from other causes unrelated to diabetes. The objective was to maximize reward for QALYs minus costs of treatment. The optimal timing of treatment for patients was determined using three published risk models for predicting cardiovascular risk. The earliest time to start statins was 40 for men, regardless of which risk model was used. However, for female patients, the earliest optimal start time varied by 10 years, depending on the risk model. Mason et al. (2010) extended this work to account for poor medication adherence. The authors used a Markov model to represent uncertain future adherence after medication was initiated. They observed that the optimal timing of statins should be up to 11 years later for patients with uncertain future adherence. However, they also found that improving adherence has a much larger effect on QALYs than delaying the timing of initiation.

Paltiel et al. (2004) constructed a simulation model to treat asthma. The model forecasts asthma-related symptoms, acute exacerbations, quality adjusted life expectancy, health-care costs, and cost-effectiveness. The authors intent is to reduce asthma manifestations, improve life quality, and reduce costs of care. The authors point out that similar models could be constructed for the control of other subpopulation-wide diseases such as obesity, smoking, and diabetes.

A great deal of work has also been done on modeling CHD interventions. Cooper et al. (2006) provide an excellent review of many models used for this disease. Most of the models reviewed by the authors are decision trees, Markov processes, or simulation models. Decisions include when and what types of interventions, and what types of drugs to employ, at various stages of disease.

### **3.1.3 Dosage of Treatment**

Given a particular treatment has been selected, the appropriate dosage must be determined. He et al. (2010) provided a discrete-state MDP model for determining gonadotropin dosages for patients undergoing in vitro fertilization-embryo transfer therapy. This work focused on patients with the chronic condition of polycystic ovaries syndrome that tend to be more sensitive to the gonadotropin treatment. The resulting policies from the MDP model are evaluated through simulation to determine the impact of misclassifying patients. In general, the use of OR techniques can be used to provide a better starting dosage with less fine tuning needed after initiation of treatment.

Dosage decisions are also important in radiation treatment planning. Several studies have focused on radiotherapy for cancer using mathematical optimization techniques. Although the vast majority of these treatment plans currently are designed by clinicians through intelligent trial and error, it is becoming essential to use optimization for extremely complicated and complex plans. Holder (2004) used linear programming for intensity modulated radiotherapy treatment (IMRT). Ferris et al. (2004) discusses various optimization tools for radiation treatment planning. In both of these papers the objective is to deliver a specified dose to the target area (above a minimum and below a maximum level of dosage) and spare or minimize damage to surrounding healthy tissue and nearby critical body structures and organs.

## **3.2 Organ Transplants**

End-stage liver disease (ESLD) and end-stage renal disease (ESRD) have received a great deal of study in the OR literature. They are chronic conditions that can result in patients eventually needing liver or kidney transplants, respectively. Chronic liver disease or liver failure can result from many causes, including liver cancer and chronic hepatitis. Often, initial treatment of liver failure attempts to manage the underlying cause, followed by intensive care and management of complications such as bleeding problems. If patients continue to deteriorate to ESLD, liver transplantation may be the

only option. Patients with chronic kidney disease have a continuing loss of renal function, leading to ESRD. Once a patient has end stage renal disease, renal replacement therapy in the form of dialysis or kidney transplantation is necessary.

While organ transplants are the best long-term solution for patients with chronic liver or kidney disease, there is a shortage of organs for transplant and a growing waiting list of patients. OR techniques have been applied to optimize the allocation of organs and timing of transplants for increasing quality and length of life of the recipients. Allocation of kidneys and livers for transplantation are challenging because both living and cadaveric donors are possible. With living donors, there is more flexibility in the timing of the transplant, allowing for the transplant timing decision to be optimized. For both kidney and liver transplantation, there are challenging decisions about whether to use a living or cadaveric donor (if both are available), and when the transplant should occur. OR techniques also aid in finding the greatest number of donor-recipient matches, considering the challenges of blood and tissue type compatibilities.

Alagoz et al. (2004) studied the question of the optimal timing of liver transplantation. They present an MDP model to find the optimal timing for a patient to have a transplant from a living donor. The patients transition through health states defined by a scoring system for end-stage liver disease. With the donor assumed to be available at any time, the MDP maximizes the patient's quality adjusted lifetime – striking a balance between having the transplant before the patient becomes too sick and waiting long enough due to the limited amount of time a patient can live after a transplant.

Su and Zenios (2004) present an M/M/1 queueing model to determine if incorporating patient choice into allocation will improve efficiency and reduce waste of organs offered to patients but not accepted. Their model incorporates uncertain arrival of patients and organs, with the service process being the kidney transplant. Since organs cannot be stored, the service time is given by the interarrival time of organs. In addition to the traditional M/M/1 assumptions, each organ has a reward corresponding to its quality, and patients may reject an organ they believe has poor quality. The authors found that a first-come-first-serve policy can lead patients to refuse organs of lesser quality, leading to waste of up to 15% of organs. They also found that last-come-first-serve (LCFS) allocation lowers the wasteful effect of patient preference. While LCFS is not a feasible rule to implement, their results highlight the need for adjustment of incentives associated with patient

choice to prevent wasting organs.

A common way for patients to find organ donors is to ask willing family members or friends to be tested for compatibility. Another area, where OR has contributed, considers patients with willing donors that are not matches. Gentry et al. (2009) considered the problem of paired kidney donation, matching two incompatible pairs with each other resulting in two successful transplants. The study considered a graph theory representation of the problem with incompatible patient-donor pairs being the vertices and two compatible pairs being represented with an edge. The maximum edge-weight matching of the patient-donor pairs graph was found, considering geographic distance between pairs and the expected lifespan after transplant. The authors show this solution does not guarantee a maximum cardinality matching. They further propose an edge-weighting that ensures maximum weight matchings also have maximum cardinality.

## 4 Emerging Applications

Rapid advances in medicine are driving new OR research opportunities. As evidence of this, over the period from 2000–2010 the total number of health care related presentations at the Institute for Operations Research and Management Science (INFORMS) annual meeting has grown from 35 in 2000 to 281 in 2009 (Denton and Verter 2010). In this section we provide some specific examples of emerging areas of research.

### 4.1 Personalized Medicine

With the sequencing of the human genome, and many recent advances in biomarkers for certain diseases, the idea of personalized medicine has received a great deal of attention in recent years. There are some examples of successful applications of personalized medicine, such as breast cancer treatment. However, for most diseases even basic risk factors are not yet considered as part of the standard guidelines. For example, gender is a well known risk factor for heart disease and stroke. While this has been known for decades, in many countries, such as the US, the published treatment guidelines for control of risk factors such as cholesterol and blood pressure are the same for men and women. These examples point to opportunities to improve the design of screening and treatment guidelines through consideration of individual patient risk factors.

## 4.2 Decision Aids

The use of OR techniques in the development of decision aids is not as wide as in other areas of treatment choices. This is an area of research that must expand if OR models are to be translated into practice. Previous work has attempted to use artificial intelligence, and computer science/information systems to provide decision support to the physician and/or patient. However, many clinicians still hesitate to use models for diagnosis or treatment. There are many possible reasons for the slow diffusion into practice. An important present and future goal is the study of the clinician-model interface. In spite of adoption difficulties, there are good examples of where OR has contributed significantly to treatment decisions. Following are several examples.

White III et al. (1982) present a quantitative model for diagnosing medical complaints in an ambulatory setting with the goal of reducing costs and improving quality of diagnoses. The development of the model is influenced by three methods: decision analysis, partially observed semi-Markov decision process models, and multi-objective optimization therapy (MOOT). The authors used an approach with Bayesian-based modeling of disease progression, resorting to the use of heuristics (a single-stage decision tree that reduces the amount of computation time and storage space per patient) to consider individual patient and physician preferences. For the MOOT heuristic, the list of possible diagnosis tests are provided, highlighting nondominated tests. The authors present a detailed example of the decision aid to treat a patient in an ambulatory setting.

Current policies related to health information exchanges assume patients want to explicitly decide who can have access to their medical records. Marquard and Brennan (2009) tested this assumption by questioning 31 patients from a neurology clinic about their willingness to share information about their medication with a primary care physician, a neurologist, and an emergency room physician. Almost all patients decided to share their current medication usage with all three doctors citing the potential clinical care benefits. However, not all patients understood the possible effects of sharing this information. The use of realistic decision scenarios and structured conversations used in this study are likely to reveal more true patient preferences than abstract opinion surveys that are commonly used in practice. In addition to correctly identifying patient preferences, it is important to assess patient understanding of the consequences of their choices. Understanding the true willingness of patients to share health information is an important step in the development

of decision aids and the inclusion of patient choices in medical decisions. Other related work uses human factors techniques to design and evaluate consumer health informatics interventions that allow patients to take part in their care, particularly for patients with chronic conditions such as diabetes.

Using multi-attribute utility theory, Simon (2009) considered the choice of treatments for prostate cancer including surgery, external beam radiation, brachytherapy, and no treatment. The model used data collected from the medical literature to compute probabilities regarding the likelihood of death and other side effects for each of the choices. Next, the model incorporated the patient's individual preferences regarding length of life and quality of life in view of the possible side effects (impotence, incontinence, and toxicity). With this data entered, the model evaluates each treatment alternative and compares the results for the particular patient.

### **4.3 Real Time Decision Making**

Many medical treatment decisions must be made in real time. Depending on the particular application, the definition of real time could be anything from a few seconds to several minutes. Such applications can be highly demanding often trading off the need for high quality decisions with available computation time.

One area in which OR has contributed to real time decision making is blood glucose control in patients with diabetes. Patients with type 1 diabetes are insulin dependent, and careful control of blood glucose within defined physiological limits is necessary to avoid a potentially life threatening occurrence of hypoglycemia (very low blood glucose that can lead to coma and/or death if not treated immediately). Blood glucose levels can change significantly over very short periods of time (seconds) depending on a variety of factors, such as caloric intake. The most common treatment for patients with type 1 diabetes is to inject insulin. However, the need for regular injection has a serious impact on a patient's quality of life. Therefore active research is being carried out on the design of closed loop control algorithms that could enable an implantable device to optimize insulin delivery (Parker et al. 2001).

Outpatient procedures can also pose a series of challenging decisions that must be made in real time (minutes). For instance, radiation treatment for cancer patients involves a series of complex decisions that can influence the effectiveness of treatment. One example is brachytherapy

for prostate cancer treatment, which involves the implantation of radioactive seeds in close proximity to a tumor. The method of brachytherapy is to place seeds in and around a tumor such that dual goals of maximizing dose to the tumor and minimizing dose to healthy tissue are balanced. Due to changes that occur in tumor size and shape and the physical movement of healthy tissue and organs in proximity to the tumor over short time periods such decisions must be made in real time at the point of placement. This real time analysis selects the actual placements of the seeds in the prostate from the thousands of possible locations, millimeters apart. Lee and Zaider (2008) present a nonlinear mathematical programming model to make location decision using real time imaging information. They demonstrate a practical application in which the clinical goals of reduced complications (e.g. impotence, incontinence) and reduced costs (\$5,600 per patient) were achieved.

## 5 Conclusions

The use of OR for the study of disease treatment and screening methods has a long history. Furthermore, recent advances in medicine are creating new challenges which are in turn resulting in new applications of OR, and new methods. This chapter surveyed some of the significant contributions of OR methods, including mathematical programming, dynamic programming, and simulation. We discussed contributions of OR to disease prevention and screening, long term management of chronic conditions, and several emerging application areas for OR.

In this chapter, we point out many examples of successful OR applications in recent decades and also many challenges that must be overcome in the future. For instance, the availability of data for analyzing medical decisions is often more complex compared to other industries. This is true for a variety of reasons including confidentiality concerns and the fragmented nature of health care delivery, and thus information systems. There are also challenges related to the fundamental difficulty in measuring criteria related to medical decision making, such as the “cost” to the patient as a result of a burdensome treatment plan. Finally, as discussed previously, there have been significant challenges in the translation of OR models from theory to practice.

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