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# Scope, Opportunities and Challenges for Operations Research in Medical Decision Making Problems

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***Abstract:*** *In recent decades there have been many advances in methods for the prevention, diagnosis, and treatment of diseases. These advances have resulted in improved health care for many patients, including longer lifespan and a better quality of life. They have also increased the complexity of medical decisions and created an opportunity for industrial and systems engineering (ISE) and operations research (OR) methods to assist medical decision making. This article summarizes some of the active areas of research and describes several examples of open problems.*

***Keywords:*** *Medical decision making, disease screening, treatment*

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## I. Introduction:

Many advances have been made in methods for preventing, diagnosing, and treating diseases. These new innovations have resulted in increased life expectancy and improvements in the quality of life for many patients. However, they have also increased the complexity of medical decision making. In many cases physicians and patients must balance the potential harm and benefit of medical interventions. Often the complexity of these decisions is compounded by uncertainty in future outcomes such as adverse events associated with diagnostic tests or long term effects of treatment. As a result of these challenges there are numerous opportunities for the application of industrial and systems engineering (ISE) and operations research (OR) methods to assist in medical decision making. Historically, medicine has been an empirical scientific discipline, centered around hypothesis generation and testing through randomized control trials (RCTs). However, not all research questions can be answered through RCTs. For instance, RCTs are often too costly to conduct, deemed unethical by institutional internal review boards, or subject to unavoidable sources of bias. Furthermore, in some cases the time required to conduct an RCT is prohibitive due to the likelihood of changes in standards of care or other factors that may confound the results of an RCT.

As a result of challenges in conducting RCTs, and the recent availability of unprecedented amounts of data about the disease incidence and progression, the use of quantitative models is gaining acceptance. Methods such as decision analysis, Markov decision processes, mathematical programming, simulation, and statistical process control, to name a few, have found applications in medicine. This has led to emerging research opportunities for ISE and related fields to play a role in helping to advance basic knowledge in many areas of medical decision making. The purpose of this article is to highlight some examples of successful ISE applications and to point out open research challenges and opportunities related to medical decision making. It is not intended to be an exhaustive survey of the current state of the art (extensive surveys related to medical decision making can be found in Pierskalla and Brailer (1994), Brandeau et al. (2004), Schaefer et al. (2004), Zhang et al. (2011)). Rather, this article provides some specific examples of recent research and emerging opportunities related to the prevention, detection, and treatment of diseases. The remainder of this article is organized as follows. In Section 2 we present several examples of stakeholders in the decision making process. In Sections 3 to 5 we provide examples of ISE methods applied to disease prevention, detection, and treatment decisions, respectively. In Section 6 we give some examples of ISE methods that have been translated into practice. Finally, in Section 7 we present some conclusions about the state of current research along with opportunities for the future.

## II. Review of Literature:

An area that has received considerable attention among OR scholars is workforce scheduling, and in particular, nurse rostering. The problem of working hours of construction for nurses to meet fluctuations in demand is extremely difficult. Service plans must comply with the requirements of the work of nurses distinguish permanent and temporary staff are qualified to provide holidays and day, night and nurses evenly over the weekend and set preferences for class officers. Linear, mixed integer and goal programming with constraint programming methods have been developed to generate nurse rosters [6]. Reviews of literature on nurse rostering are available in Burke et al. [7] and Lim et al. [8]. Appointment scheduling has also been a rich research area over the past decades (e.g. see Gupta and Denton [9]). The process of assigning time slots for serving out- and inpatients arises in diagnostic and treatment units deals with uncertain service times, no-shows, cancelations, and walk-ins. A good appointment schedule keeps patient waiting times short and minimizes staff overtime taking into account the patient load and the available resources (i.e. staff, rooms, and equipment)? In view of this numerous authors developed models with the objective of i. How many patients to schedule? ii. How to allocate appointment slots throughout working day? iii. What is the optimal sequencing of heterogeneous patients? Recently, Granja et al. [10] developed an optimization model based on simulation approach to the patient admission scheduling problem using a linear programming algorithm. Richard et al. [11] provided an improved method for solving the so-called dynamic patient admission scheduling (DPAS) problem. Atlie et al. [12] presented an exact method for Patient Admission Scheduling (PAS) problem based on a recursive logic-based Benders' decomposition where each sub problem is formulated as an integer linear program. Turhan et al. [13] addressed two Mixed Integer Programming based heuristics namely Fix-and-Relax and Fix-and-Optimize where PAS problem instances are decomposed into sub-problems and then the sub problems are optimized. Kidney dialysis therapy initiation for evaluating cost and effectiveness is investigated in Lee et al. [14]. They used Approximate Dynamic Programming and Simulation to determine an optimal therapy and a strategy for maximizing patient welfare. Chen [15] proposed the kidney allocation problem. He assumed that the decision has to be made within a fixed time horizon because a kidney is perishable and the kidneys are limited. He addressed that the objective of kidney allocation problem is to determine the allocation rule to maximize the total expected value achieved. The arrival, demand pattern of patients is random. When we replace kidneys with airline tickets and patients with travelers, we get the airline yield management problem. When we replace kidney and patient by job and worker respectively, it has the typical scheduling problem. Recently, Thamer et al. [16] developed a risk score to assist shared decision making for kidney dialysis initiation. Then Bagshaw et al. [17] addressed strategies for the optimal timing to start renal replacement therapy in critically ill patients with acute kidney injury Operating theater planning and scheduling (OTPS) has also received much attention in the past 60 years. The strategic (long term) planning level addresses capacity planning given a forecast of patient demand. Typically, the operating theaters and the time allocated to each activity of the department at the time. The tactical (mid-term) planning level deals with the creation of weekly/monthly (rough) schedules for elective surgeries. Operational planning, the operational plan for the next day, generating a sequence of operations in each operating room early and distribution activities and some resources. Finally, the online planning level deals with rescheduling previously planned surgeries as a result of unforeseen events such as delays, emergencies, and cancelations. The rich and still growing literature on OTPS covers a wide range of OR methodologies (heuristic approaches, and simulation) for deterministic and stochastic environments [6]. Reviews of literature up to 2010 on Operating Theater planning and scheduling are available in Cardoen et al. [18]. Recently, Wang et al. [19] investigated an operating theater allocation problem with uncertain surgery duration and emergency demand. In Wang et al. [19], the operating room allocation problem with cancellation risk is mathematically formulated as follows:

$$J = \sum_{r \in R} c^f x_r + c^t E_w \left( \sum_{r \in R} O_r^w \right)$$

subject to

$$y_{ir} \le x_r \quad \forall i \in I, \forall r \in R$$

$$\sum_{r \in R} y_{ir} = 1 \ \forall i \in I$$

$$O_r^w = \left( \sum_{i \in I} y_{ir} d_i^w + e_r^w - T \right)^+ \quad \forall r \in R, \forall w \in \Omega$$

$$P\left( \sum_{i \in I} y_{ir} d_i + e_r > T + H \right) \le \beta \ \forall r \in R$$

$$x_r, y_{ir} \in \{0,1\} \ \ \forall i \in I, \forall r \in R$$

Strategic operating theater planning belongs to the group of resource allocation and capacity planning problems. This group involves decisions concerning the mix and volume of patients treated by a hospital and the amount, capability, and type of resources for the delivery of healthcare. Hospital layout planning is also at the strategic level, but has received much less attention. The goal is to design a hospital, a clinic or a department in order to minimize the movements of patients and accompanying resources such as medical staff and equipment [6]. Quadratic integer programming models were proposed by Butler et al. [19] and Elshafei [20] for problems arising in this area. Patient transportation is a variant of the dial-a-ride problem (DARP) and concerns finding a set of minimum-cost routes and schedules for a feet of ambulances (or hospital staff) to transport (or escort) inpatients between nursing wards and diagnostic units. Hospital-specific constraints (e.g. different priorities of requests, needs special equipment and support medical staff during transport and handling of incomplete knowledge in advance) significantly complicate the development of high-quality vehicle routes and schedules. The latter is often controlled by the imposition of the travel time of the patient and minimizing deviations from the desired times for pickup and delivery [21]. By its nature DARP combined extremely difficult to solve, which has contributed to the development of new OR, in particular the new (meta-) heuristic methods allowed [6]. Beaudry et al. [22] and Kergosien et al. [23] proposed tabu search based approaches, while Hanne et al. [24] embedded an evolutionary algorithm in a software application designed to support all phases of the transportation flow including request booking, scheduling, dispatching, monitoring, and reporting. Recently, Knyazkov et al. [25] illustrated the evaluation of Dynamic Ambulance Routing for the Transportation of Patients with Acute Coronary Syndrome in Saint-petersburg. Zhang et al. [26] addressed a real-life public patient transportation problem derived from the Hong Kong Hospital Authority (HKHA), which provides ambulance transportation services for disabled and elderly patients from one location to another. Aiming at improving the efficiency and reliability of ambulance service, several location models for ambulance stations have been proposed in the OR literature. Well-known approaches to this problem are coverage model and median model. Coverage model looks for the location to maximize the (deterministic or probabilistic) covered demand of ambulance calls. Hence this model can be thought of reliability oriented model. On the other hand in median model the objective is to minimize the total traveling distance of the ambulances from the station to the scene of call. This model gives more weight to the efficiency of ambulance operation [27]. Morohosi [27] addressed the comparison of those optimization models through actual patient call data from Tokyo metropolitan area to show the characteristics of each model and investigate a possibility of improvement in ambulance service. Problem of patients overflow in wards is addressed by Teow [24] The demand of hospital's inpatient beds by medical specialties changes according to patients' volume over time. With no adjustments to the allocation of beds, the growing mismatch will result in unnecessary patients' overflow. This will lead to poor patient care, travel health workers redundant and the waiting bed. Hence, hospitals need to periodically review their bed allocation by specialties. The bed reallocation exercise is typically a zero-sum game: some specialties will end up with more beds while others with fewer beds. Teow [24] suggested the structure of the patients overflow problem. He first established bed demand for each specialty using patientday. He stated that the objective of the problem is to assign the beds (i.e. decision variables) such that the specialties will end up with equitable bed occupancy rates (i.e. outcome), subject to number of beds available (i.e. constraint). Litvak et al. [28] presented a mathematical method for computing the number of regional beds for any given acceptance rate. In Litvak et al. [29], for blocking probability, they computed the famous Erlang loss formula

$$B(c, \rho) = \rho^c / c! \Big/ \sum_{k=0}^{c} \rho^k / k! \text{ where } \rho = \lambda \mu^{-1}$$

is the load, with λ the call arrival rate, and μ-1 the mean call length based Equivalent Random Method (ERM), and they schematically depicted (Figure1) the patient flows for two ICUs (Figure 1).

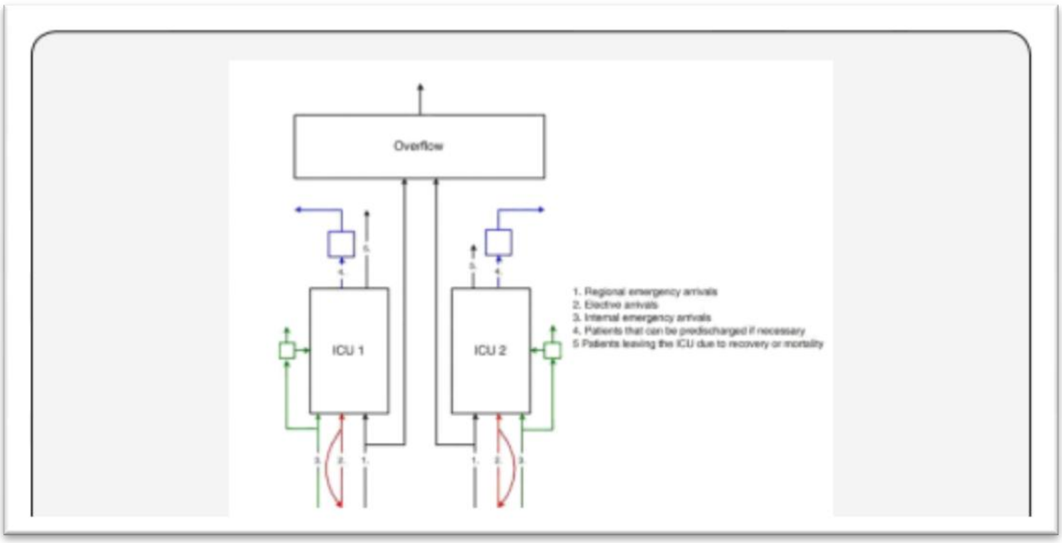


**Figure 1:** Overview of the ERM including all patient streams [28].

Outpatient appointment scheduling in health care has been researched over the last 50 years. Various scheduling rules have been proposed in different research works Bailey [30]. A good appointment schedule is one that trade-offs patients waiting time for clinics overtime, constrained by the patient load and staffing. Operations research researchers use techniques such as queueing theory and discrete event simulation to propose various appointment strategies under different clinics settings. Some planning strategies can be very complex. Although the list of applications for logistics and research hospital management operation is far from over, above shows the range of possibilities in the field of operations research in hospitals [29].

## III. Decision Maker Perspectives:

Applications of ISE methods to medical decision making often seek to find an optimal choice among alternatives. For example, selecting the best sequence of screening tests to diagnose a disease, or the best medication regimen or surgical intervention to treat or cure a disease. These problems require an explicit definition of the criteria associated with the decisions. The criteria are determined by the stakeholder perspective. In medical decision making there are four commonly considered perspectives: patient, physician, third party payer, and societal. The criteria of the stakeholder are influenced by the health system in which they reside. For example, if patients have third-party health insurance that covers all or most healthcare expenditures, then the most relevant criteria are those related to the effects of treatment. Treatment effects can be positive (longer life expectancy, a reduction in chronic conditions, or improved quality of life) or negative (short-orlong term side effects, disablement, or death). A common way to quantify the tradeoff between the pros and cons of treatment is through the use of quality adjusted life years (QALYS), which is a numeric measure for a year of life between 0 (death) and 1 (perfect health). Estimates of QALYs can be elicited through patient surveys and are commonly used for treatment evaluation and health policy investigations (see Packer (1968) and Fanshel and Bush (1970) for a review of the use of QALYs). The physician perspective is often assumed to be aligned with that of the patient. In practice, decisions are often made through a shared patient-physician decision making process. When third-party payer or societal perspectives are considered, costs become part of the criteria. The decision of which costs to include in a study can be challenging, For example, costs may include the direct cost of drug treatment, hospital billing for procedures, the cost of follow-up visits to monitor treatment (e.g., laboratory testing of cholesterol levels following initiation of cholesterol lowering medication), or to evaluate recovery (e.g., outpatient visits to a surgeon in the weeks and months following surgery). In some cases the cost burden may be on members of a patient’s family and friends, or on a patient’s employer due to leave from work. From the third-party payer perspective there is a tradeoff between the immediate cost of medical treatment (e.g., blood pressure lowering medications) and long term potential cost savings associated with avoiding serious health outcomes (e.g., heart attack or stroke). The societal perspective, which simultaneously considers the patient, physician, and third-part payer perspectives, involves the consideration of multiple criteria. Quantitative analysis requires a factor, sometimes referred to as willingness-to-pay, which defines the monetary value of QALYs. A commonly used estimate in the U.S. is $50,0000/QALY; however, the most appropriate value is widely debated (Rascati, 2006). Often researchers will explicitly consider multiple criteria and employ the concept of an efficient frontier to determine candidate solutions that are not dominated. Identifying the gap between the optimal solution for the patient/physician and the third-party payer perspective informs the debate about optimal decision making.

**Disease prevention**

The benefits of disease prevention are summarized by the idiom “an ounce of prevention is worth a pound of cure.” Advances in the state of knowledge about risk factors for disease have created new opportunities to help individuals avoid or delay disease onset and progression. However, these advances have also added to the complexity of medical decisions. ISE methods can assist in making decisions about how best to prioritize risk factors, select preventative treatment options, and estimate the effects of prevention programs for individual patients as well as for entire populations. An important aspect of prevention is educating patients about risk factors such as smoking, obesity, cholesterol, and blood pressure control. All of the above are well established risk factors for cardiovascular disease, a leading cause of death in many parts of the world. While the benefits of controlling risk factors are clear, success in prevention at the population level can be costly. For many patients, their primary care physician is the likely source of information about the importance of prevention. However, physician time is costly and limited, leaving decision makers with the open questions of how to prioritize educational activities and how to optimize the timing of interventions. Mason et al. (2011) studied the benefits of adherence improving educational interventions in the context of cholesterol lowering medications. The authors found that the optimal time to initiate statin treatment is influenced by the likelihood of patient adherence. They present cost-effectiveness analysis on the evaluation of hypothetical adherence improving interventions designed to improve the likelihood a patient takes their daily dose of medication. They find that interventions can increase expected QALYs for patients, and may reduce overall costs to the health system by avoiding costly health outcomes. Vaccination is another important topic that is central to disease prevention. There are many challenges related to the delivery of vaccines to a population. First, there are often multiple delivery methods including monovalent and multivalent vaccines with varying costs and benefits. Second, some vaccines have conflicts with others and some have special scheduling requirements, such as multiple doses that must be administered within a minimum or maximum time window. Third, for some diseases there is uncertainty about the future evolution of epidemic strains, resulting in questions about selecting the best design. 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 the design of vaccination schedules. Jacobson et al. (1999) proposed an integer programming model with the goal of finding the lowest cost formulary subject to constraints based on clinical recommendations for childhood immunization. Some diseases, such as seasonal flu, evolve over time, necessitating regular vaccination. This leads to challenging decisions about how to design vaccines. For example, Wu et al. (2005) proposed a continuous-state discrete-time dynamic programming model for the design of the annual flu vaccine. In their model, 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 represents the efficacy of the vaccine. Researchers have also contributed to problems related to the intentional infection of a population. For instance, Kaplan et al. (2003) analyzed bio-terror response logistics using smallpox as an example. The authors developed a system of ordinary differential equations (ODEs) incorporating scarce vaccination resources and queueing of people for vaccination. Controlling risk factors over the course of a patient’s lifetime is important for preventing some common chronic diseases. For example, high cholesterol and blood pressure increase the likelihood of heart disease. Better control of these factors may help avoid or delay heart attack and stroke. Common interventions involve improvements in lifestyle (e.g., diet and exercise) or the use of medication. In recent decades numerous medications have come on the market such as statins for cholesterol control, and ACE inhibitors for blood pressure control. Trading, off the benefits and costs of these medications can be challenging and depends on the decision maker’s perspective. From the patient perspective the benefits are a reduced probability of heart attack and stroke; however, this must be assessed against the downside of medication including patient copy, side effects, and possible consequences of long term exposure to the drug. From the third-party payer perspective, considerations include the full cost of medication, which can vary widely depending on whether it is a generic or a brand name, and the cost savings from avoiding major health outcomes such as heart attack and stroke, including immediate costs of emergency care, and long-term follow-up costs.

**Treatment decisions**

Many diseases now have treatment options that can cure or delay the progression of the disease. In some cases treatment decisions are one-time decisions, but in other cases treatment decisions recur, often involving the coordination of multiple treatment types to achieve control of one or more risk factors. Liver transplant decisions, often treated as one-time decisions, have received significant attention in the ISE literature. In the case of live donor transplants, such as liver transplants, there exists an optimal timing decision that involves maximizing the pre- and post-transplant lifespan of an individual patient. Alagoz et al. (2004) studied a Markov decision process to maximize expected quality adjusted lifespan of patients with end stage liver disease. The states of their model were defined by the patient’s health states. The authors establish a number of structural properties, including the existence of an optimal threshold type policy. Results are presented based on model parameter estimates from a large population of patients with end stage liver disease. In some cases there are multiple treatments, with different advantages and disadvantages. One example is prostate cancer, which can be treated with prostatectomy (surgical removal of the prostate), external beam radiation, brachytherapy (implantation of radioactive seeds in the prostate), and active surveillance. Active surveillance is a recent treatment protocol that can involve medical treatment and regular biopsies to monitor the progression. Sanda and Kaplan (2009) provide an excellent description of the decision process for a particular patient diagnosed with low risk prostate cancer. The authors point out that there is no single treatment option that is uniformly considered to be the best. Rather, the decision maker must consider many factors including the risk of mortality from treatment, variation in the likelihood of future recurrence, and the side effects of treatment including sexual dysfunction and urinary incontinence. Many diseases involve complex drug treatment decisions, particularly chronic conditions for which treatment decisions are made over long time frames. For example, patients with diabetes must carefully weigh the costs and benefits associated with treatment of multiple risk factors including blood sugar, blood pressure, and cholesterol control. Mason et al. (2011) use an MDP model to study the optimal timing of treatment options under uncertainty about future health states. Simultaneous control of multiple risk factors presents challenges, including a combinatorially large health state space resulting from the dependence of health states on treatment history. Another important application area is the design of intensity modulated radiation therapy (IMRT) plans for the treatment of cancer. Such planning problems involve decisions such as the optimal selection and intensity of external beams with the goal of balancing the goals of ensuring a high dose to the tumor while minimizing radiation close to critical structures. The design process naturally divides into three sub-problems, those being:

1) The selection of the beams that will be used in the treatment,
2) Deciding on the amount of radiation to deliver along those beams, and
3) Optimizing the delivery of the treatment. The preponderance of the literature addresses one of the three problems, but the modern trend is to combine these to better optimize the overall treatment, see Matthias et al. (2008) for a detailed discussion of these topics.

## IV. Open Opportunities:

New trends in medicine will provide opportunities for the development and application of ISE methods, and we identify several examples of emerging research areas.

**Personalized medicine**

Personalized medicine, which is noted to be the future of medicine Liebman (2007), emphasizes the customization of healthcare interventions for individual patients using each person's unique clinical, genetic, genomic, and environmental information. Personalized medicine may lead to alternative interventions for patients and therefore may require the use of advanced mathematical modeling such as large-scale optimization to choose the best intervention. For instance, as Alagoz (2011) notes, the use of personalized medicine will increase the number of possible cancer screening policies (i.e., specification of what age to start and end screening and how often to screen) that need to be evaluated. With the sequencing of the human genome and the desire to detect hard-to-treat diseases for early and successful intervention (e.g., pancreatic cancers, brain tumors, Alzheimers' Disease), biomarkers are developing rapidly. Feltus et al. (2003) described predictive models for early cancer diagnosis. Mathematical programming techniques can also be powerful tools for classification and disease prediction (Lee and Wu, 2007). However, significant challenges remain in the solution strategies for large-scale and multi-group instances.

**Patient behavior**

An important issue in medical decision making understands the influence of patient behavior. One example is patient compliance to medical recommendations, which can significantly influence any recommendations about medical decisions. As World Health Organization (WHO, 2003) reports, "Adherence to therapies is a primary determinant of treatment success. Poor adherence attenuates optimum clinical benefits and therefore reduces the overall effectiveness of health systems." It is therefore crucial to consider the effect of poor adherence in optimizing medical decisions and tailoring clinical recommendations based on patient behavior. Patient behavior can mean more than just compliance and adherence. There is significant research being done by clinicians and social scientists on behavioral models. This is also a potential area of application for ISE methods where medical and behavioral sciences need to be integrated. In particular, there is a need to develop mathematical models that represent human behavior to better understand its role in medical decision making.

**Natural history of disease**

Most medical decision making studies require data-driven mathematical models to represent the progression of a particular disease without any intervention, i.e., the natural history of a disease if left untreated. Because there is typically no clinical data about the natural history of diseases such as breast cancer or end stage liver diseases, it is necessary to develop and use a theoretical natural history model. Such models often require calibration using observational data that is often influenced by various sources of bias. The accurate estimation of the natural history of a particular disease based on observational data is important since it establishes a baseline. However, little research has been done to develop generalizable approaches that use observational data. In the future ISE methods may provide ways to estimate natural history models.

**Future medical interventions**

Most medical decision making studies estimate disease progression and treatment outcomes using current available treatment options, and they assume that treatment options remain constant in the future. On the other hand, medical research and development often leads to new and improved therapies, such as in HIV and organ transplantation. As a result, in some cases where innovations are anticipated in the near future ISE studies using stochastic models in medical decision making such as Shechter et al. (2010) are needed to consider how the uncertain availability may affect decisions.

## V. Conclusion:

This article summarizes active areas of research and open challenges for future research related to the applications of ISE methods to medical decision making. Among the future challenges will be the development of new models for capturing personalized genetic information, patient behavior, and the integration of decisions related to prevention, detection, and treatment. These new directions are anticipated to lead to practical applications that improve the health and quality of life of patients and the efficiency of health systems. These new research directions also hold the promise of new methodologies that can be directed to other important problems.

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