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## Operations research and health systems: A literature review

Samar Shetaban<sup>1</sup>, Mir Mehdi Seyyed Esfahani<sup>2</sup>, Abbas Saghaei<sup>1</sup>, Abbas Ahmadi<sup>2</sup>

### Abstract

Today's human health is in the best situation ever. The progress of vaccines, development of hospitals, new medicines, advanced medical equipment, and new treatments preventing death will place the health system indicators at its best state in all ages and centuries. In addition, healthcare is one of the biggest industries in developed and developing countries and is a service-oriented industry that is significant, high-quality, and safe in medical services. Healthcare has become one of the biggest sectors in terms of income and employment. Health care involves hospitals, medical devices, clinical trials, outsourcing, telemedicine, medical tourism, health insurance, and medical equipment. Nowadays, the application of operations research in various fields, including health, is on increase. Although many issues face operations research in healthcare, such issues are not analytically different from the issues in other industries. Operations research, as a quantitative systemic method, can considerably solve the problems related to the health system. The present study aimed to evaluate the application of operations research models based on the research process in health systems including Markov decision-making processes (MDPs) and partially observable Markov decision process (POMDP), etc., and compare these methods with each other. The basis of this study was evaluating the publication of scientific studies on operations research models in the health systems.

**Keywords:** operations research; health systems; research process; Markov model.

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## 1. Introduction

Nowadays, changes in lifestyle, cultural and social structure, medical needs, public health, and rapid population growth have caused serious problems to the supply of healthcare facilities and services. The rapid increase of healthcare services costs is so high that controlling such costs is a major problem for the health care systems in various countries even in rich countries. Since a healthy human being is known as the axis of sustainable development, the health system and its subsystems are among the most significant pillars of the development of society. The effective and efficient management of various parts of the health system and effective allocation of resources to needs are among the old challenges of researchers and managers in this field. In addition, healthcare is one of the biggest industries in developed and developing countries and is also a service-oriented industry. This is a considerable service industry which

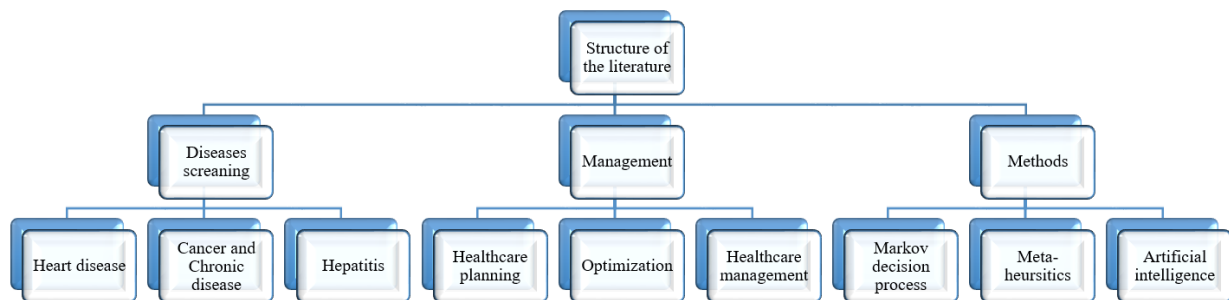
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\* Corresponding author; [msefahani@aut.ac.ir](mailto:msefahani@aut.ac.ir)

<sup>1</sup> Department of Industrial Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran.

<sup>2</sup> Department of Industrial Engineering, Amirkabir University of Technology, Tehran, Iran.

is significant, high-quality, and safe in medical services. Healthcare has become one of the biggest sectors in terms of income and employment (WHO, 2007). Healthcare involves hospitals, medical devices, clinical trials, outsourcing, telemedicine, medical tourism, health insurance, and medical equipment. Although many issues face operations research in healthcare, such issues are not analytically various from the issues in other industries. Operations research, as a quantitative systemic method, can considerably solve the problems related to the health system. For this reason, this study aimed to examine the application of operations research models in this field based on three main aspects as disease screening, management, and methods which are illustrated in Figure 1.



**Figure 1. The structure of the studied literature review**

As the rest of the manuscript, Section 2 describes the classification of studies based on application types and diseases, which surveyed Operations Research (OR) techniques. In Section 3, the literature review of the methods and types of diseases is given, and finally, in Section 4, the conclusions and suggestions for future studies are presented.

## 2. Healthcare planning

The importance and significance of planning in healthcare can hardly be overemphasized today when providing proper and adequate service continues to be a key concern of most countries. For growing longevity and aging population amidst dwindling birth rates, many countries are increasingly hard-pressed for the extra budget and resources to meet the healthcare needs. Many have turned to OR for optimization and cost-control measures (Capan et al., 2017). Some of the key healthcare issues considered in OR today include estimation of future demand for services in order to build enough capacity, selection of hospital locations for covering a target population, and design of the emergency facilities for efficient handling of patients. A powerful tool for planning is a simulation (cf. Jun et al., 1999; Kok et al., 2003; Ashton et al., 2005; Eldabi et al., 2007; Jacobson, 2006; Günal and Pidd, 2009, 2010; Brandeau et al., 2004). But several other techniques have been successfully used, as shown in the following sections.

### 2.1. Demand forecasting

Accurate demand forecasting is essential in healthcare planning, its results providing the input to several optimization problems. While forecasting methods can be qualitative or quantitative, most research work has focused on quantitative analysis because of better accuracy. However, the availability of good, historical data is essential for quantitative methods.

Finarelli and Johnson (2004) gave a detailed, nine-step, quantitative demand forecasting model for healthcare services, while Cote and Tucker (2001) discussed four common methods for forecasting demand for healthcare services: percent adjustment, 12-month moving average trend line, and seasonality. The accuracies of various forecast methods were evaluated by Jones et al. (2008). They used data from daily patient arrivals at the emergency departments of three different hospitals and considered the following methods: time series regression, exponential

smoothing, and seasonal autoregressive integrated moving average and artificial neural network models.

Beech (2001) derived market-based healthcare service forecasting from a broad range of available data for estimating future demand. The data sets involve primary as well as secondary service areas, service-area populations by various demographic groupings, discharge utilization rates, market size, and market share by service lines. They found that market dynamics can allow a variety of explicit assumptions and trends for developing scenarios of potential future demand.

A two-step approach for forecasting future demand along with capacity needs was given by Myers and Green (2004). In particular, their approach develops a facility master plan incorporating the projected capacity as well as physical requirements. Xue et al. (2001) analyzed the continued growth of the end-stage renal disease population in the United States. They forecasted up to the year 2010 using historical data with stepwise autoregressive and exponential smoothing models (Rais and Viana, 2011).

In addition to traditional techniques, researchers have developed new methods for forecasting demand. These methods, which are based on artificial intelligence, try to identify a hidden relationship between inputs and outputs. This latent relationship is similar to the regression relationship or moving average but has a much higher quality than these methods (Mostafaeipour et al., 2019).

Artificial intelligence methods are closely related to optimization with meta-heuristic algorithms (Tirkolaei et al., 2019, 2020a, 2020b; Sangaiah et al., 2020). In artificial intelligence methods, the weight of biases is determined through an approximate optimization process. In this regard, the use of meta-heuristic algorithms can be a very appropriate and efficient tool to improve artificial intelligence methods in demand forecasting (Goli et al., 2019, 2020).

Jiang et al. (2017) reviewed the most important researches in the field of artificial intelligence in healthcare. They suggested three major areas for early detection and prediction in healthcare using artificial intelligence. They encouraged early detection and diagnosis, treatment, as well as outcome prediction and prognosis evaluation. He et al. (2019) proposed a developed form of artificial intelligence for demand prediction in medicine. Fischer et al. (2020) used artificial intelligence for data prediction in small hospitals. Moreover, they introduced an efficient model based on demand prediction to allocate medical staff to different stages.

## **2.2. Location selection**

Location selection is one of the most important decisions and strategies that has a great impact on the quality of the performance of the medical system. The location of health centers has been studied in both normal and critical conditions. Under normal circumstances, the goal is to establish small and large hospitals so that the demand for treatment can be fairly distributed among the various centers. In times of crisis, the goal is to locate relief centers temporarily and on an outpatient basis so that relief time is reduced (Davoodi & Goli, 2019).

A large body of publications in healthcare addressed various issues concerning capacity management and location selection, both for healthcare services and medical material (see, e.g. Ndiaye and Alfares, 2008; Araz et al., 2007; Bruni et al., 2006; Rauner and Bajmoczy, 2003; Neter et al., 2003; Verter and Lapierre, 2002; Arruda et al., 2018). Daskin and Dean (2004) reviewed location set covering, maximal covering, and P-median models for addressing the location planning issues in healthcare. They presented a novel application of the set covering model for analyzing cytological samples. Additional review of location models in healthcare can be found in Smith-Daniels et al. (1988). A review of location and allocation models restricted to developing countries can be found in Rahman and Smith (2000).

Where to set healthcare centers for maximizing accessibility has been extensively studied by OR practitioners. Location problems arising in developing countries have been discussed by several authors. Smith et al. (2009) studied the planning of sustainable community healthcare in the rural areas of developing countries. They considered both top-down and bottom-up hierarchical location models for the efficient planning of community health schemes and proposed a Mixed Integer Program for determining the locations of the maximum number of sustainable facilities.

Munir et al. (2019) analyzed inadequacy and equity issues in locating healthcare points in the developing area of Pakistan. They considered travel time and aggregated population as the major criteria in finding suitable points. Kaveh et al. (2020) proposed a novel framework for hospital location-allocation. They proposed a mathematical model and improved genetic algorithm to find the best locations using effective and affectability rates. Jenkins et al. (2020) developed a multi-objective integer mathematical programming formulation to determine the location and allocation of aerial medicine assets.

### **3. Literature review**

The diagnosis of liver disease requires a long time and sufficient expertise of the physician. Statistical methods can be categorized as an automatic predictive system which helps specialists to diagnose the liver disease quickly and accurately. The Hidden Markov model is an intelligent and strong statistical method being applied by Madadzadeh et al. (2016). The data applied in this study were collected in a cross-sectional way from the records of the patients with five types of liver disease. Such patients were admitted to Afzalipour Hospital in Iran from 2006 to 2013. The Hidden Markov model was applied with the help of the EM algorithm to learn, proportional to the data, to study the performance of the model and measure the accuracy and sensitivity. The results of this study indicated the potential capabilities of the hidden Markov model. Thus, using the hidden Markov model is suggested for predicting the diagnosis of liver disease. Belciug and Gorunescu (2020) described the advantages of using intelligent decision support systems in medical studies. Intelligent decision support systems help the healthcare system through the better diagnosis of the appropriate treatment plan, improvement of hospital management, and some insurance frauds. Data scientists around the world develop more machine learning techniques that extend the quality of life. Breast cancer is one of the most common types of cancer in the U.S. (Ayer et al., 2012, 2015; Erenay et al., 2014). Many decisions should be made by a physician or patient while dealing with potential breast cancer. Many of these decisions are made under uncertainty whether this uncertainty is related to the patient's health progress or the accuracy of the physician's tests. Any possible action can have positive effects, including surgery which removes a tumor and eliminates the negative complications including postoperative infection successfully. The human mind cannot easily consider all of the involved variables and possible results while making decisions. In the study conducted by Hudson (2019), a partially observable Markov decision process (POMDP) was presented for screening breast cancer. The required parameters were created for the first time using the related medical literature and stimulating the patient's records. Then, the POMDP was optimally solved using the Perseus algorithm for an unlimited horizon. Such a policy led to several recommendations for screening breast cancer. Based on the results, clinical breast examinations are significant for screening young women. Based on the decision of surgery on a woman with breast cancer, the policy revealed that invasive cancers with a brain tumor more than 1.5 cm or in metastasis should be removed as soon as possible. However, the patients who are confident with being healthy should have a breast biopsy. The cause of this error was studied more and it was concluded that a limited horizon may be more appropriate for this program. About 13% of the adult population in the world was obese in 2016 and the prevalence of obesity has increased during recent decades. The increased risk of cancer is one

of the consequences of obesity. In a study by Yaylali and Karamustafa (2019), the BMI-based obesity levels modeled cancer and death using a Markov decision process to observe the effect of obesity on cancer and mortality risks.

Such a model aims to evaluate the modified quality of life and stimulate a person's longevity from 20 to 70 years. The measures which are available to decision-makers have no intervention with obesity. Obesity surgery is one of the most effective methods for preventing obesity and is particularly recommended for patients with obesity. However, this disease is related to the enhanced risk of mortality. This model aims to observe the complex dynamic between obesity, cancer, mortality, and obesity surgery. In addition, this model was obtained using randomized clinical trials and published studies. The results indicated that obese people at all levels of obesity should undergo obesity surgery for improving their health and reducing their risk of cancer. This study has the potential of creating guidance for obese people while evaluating obesity surgery and can be increased by adding other health consequences of obesity to the model. The economic evidence of health about the value and optimal goal of genetic testing in the prevention of coronary heart disease (CHD) is limited and ambiguous (Parthiban et al., 2011). The objective of a study by Hynninen et al. (2019) was to optimize the application of population utilization and target the genetic tests along with traditional risk factors in the prevention of cardiovascular events and evaluation of the cost-benefit of genetic tests. For this purpose, several strategies were compared for the application of traditional and genetic tests in preventing CHD through statin therapy. The goal was to run some tests on various parts of the patient in these strategies using a decision-analytical model where the patient's estimated risk was updated based on test results using Bayesian methods. The data for this model was highly wide and included the national healthcare offices, the Finnish Institute for Molecular Medicine, and published literature. The results indicated that targeting the genetic tests in the optimal method was effective for the patients in whom the traditional risk factors of results failed at sufficiently providing accurate data at the highest expected net profit. In particular, the optimal application of genetic tests reduces the expected costs of a patient aged 45 or over 10 years while maintaining the expected health results compared to traditional risk factors. Such a conclusion is resistant to logical changes in the model inputs.

### **3.1. Survey on Markov decision process (MDP and POMDP)**

In the study conducted by Latha and Vetrivelan (2019), the projection of modeled heart diseases was presented using a partially observable Markov decision process (POMDP). In an emergency case, the patient is warned by Fog computing and the physician. The ambulance is sent to the patient's place in critical condition. The physician receives the data through cloud computing. Fog computing in healthcare is a new field that attracts more into the research population. A lot of studies focused on coronary heart diseases. An essential risk factor for coronary heart diseases is the increase in blood viscosity. The highly sticky nature of blood does not let the blood circulation to resist. The risk factors for heart diseases involve high blood pressure, obesity, diabetes, increased blood viscosity, etc. The POMDP model calculates the approximation of policy in projecting heart diseases. Güneş and Örmeci (2018) presented an overview of disease screening and operations research applications in various aspects of this problem. This study first discussed the applications of operations research in evaluating and optimizing the screening policies.

Cost-effectiveness analysis and personalized medical decision approach making for screening issues were evaluated in this study. The discussed methods involved microsimulation models, compartmental models, general random models, and partially observable Markov decision processes. After that, organizing the screening services was explained in order to reach the population and improve the efficiency of screening. The main topics included the problems related to location and resource allocation. Cancer screening can benefit from individual

decision-making tools that reduce over-diagnosis. The heterogeneity of participants in cancer screening requires some unique methods. The POMDPs decision protocol can be applied for indicating unique screening policies while being defined with an appropriate reward function. Nevertheless, determining an appropriate reward function can be challenging. In a study by Peterse et al. (2018), it was suggested that using inverse reinforcement learning (IRL) was appropriate for creating reward commitments for POMDP screening for lung and breast cancer. Two POMDP models with various reward functions were developed using the experts of retrospective screening decisions for lung and breast cancer screening. In particular, it was indicated that the inverse reinforcement learning algorithm was the maximum entropy to obtain a more efficient reward. POMDP screening models were evaluated based on their ability for preventing appropriate screening decisions before diagnosing cancer. The reward function was learned with the maximum entropy inverse learning reinforcement algorithm and indicated a comparable performance to experts when being combined with POMDP models in lung and breast cancer screening. Cohen's kappa score on the agreement between POMDP and the projection of physicians was high in breast cancer and indicated a decline in lung cancer. Active classification, i.e. sequential decision-making process aimed at obtaining data for classification purposes, typically emerges in many applications including medical diagnosis, intrusion detection, and object tracking. Wu et al. (2019) studied the active classification of dynamic systems with a finite set of Markov decision process models. Researchers have been interested in finding the strategies which actively interact with the dynamic system and observe its reactions in such a way that the real model is determined efficiently with high reliability. For this purpose, they presented a theoretical framework for decision-making based on partially observable Markov decision processes (POMDP). Based on an initial belief, the classification probabilities, a cost range, and a limited time horizon design POMDP strategies leading to classification decisions.

There are two various approaches to finding these strategies. The first approach calculates the "optimal strategy" exactly "by repeating the value" for overcoming the computational complexity of finding accurate solutions. The second approach is based on comparative sampling to estimate the optimal probability of reaching a classification decision. Finally, the proposed model is displayed using examples of medical diagnosis. Markov decision process models are the powerful tools that allow the derivation of optimal policy but may lead to long computational times and create the decision-making rules which can be interpreted with difficulty. In order to improve the usability and interpretability of this model, Sheller-Wolff (2018) examined if Poisson's regression could estimate the optimal blood pressure treatment policies applied by this model for maximizing the quality of life of the patient. The results indicated that Poisson's approximation was consistent at 99% compared to the optimal behavior policy. Such high accuracy leads to almost healthy results for patients. Rapid progress in healthcare for chronic diseases including coronary heart diseases, cancer and diabetes, early diagnosis, and treatment based on risk factors have made specific demographic factors and biomarkers of the disease possible (LaRosa et al., 1999). However, a lot of relevant risk factors along with uncertainty about future health complications and side effects of health interventions challenge the clinical management of diseases for physicians and patients. Research methods in data-based operations have the required potential for improving medical decision-making using the observational data being currently collected in many health systems. Optimization methods in particular, including Markov decision processes and Markov observable decision processes, have the potential of improving the long-term sequential decision process being common in many chronic diseases. Denton (2018) introduced some of the most common methods for making and solving the models of sequential decision making optimization. The texture of chronic diseases is emphasized while the methods are extensively applied to the sequential decisions which are created under uncertainty. This study paid special

attention to the challenges on the application of observable data, the effect of uncertainty on the model, and ambiguity parameters. Bonifonte (2018) studies developed analytical tools using operations research and statistical methods to solve problems in the field of coronary heart disease and blood pressure management.

Wang (2017) presented measurement value Markov decision processes (MVMDPs) and provided an algorithm for finding an optimal policy for this model. The MVMDP considers a whole range of Markov decision processes and indicates a critical feature of human thinking: Humans think about the problems and can choose his optimal actions with the probability that he understands all cases (i.e., they measure the atmosphere of the state approximately).

Therefore, the Markov decision process is the conscious result of the unconscious decision-making mind (Feinberg and Shwartz, 2012). Furthermore, it generalizes such thinking to the category of divergent thinking and provides a model of the Markov process with a value criterion based on the process of branching into a criterion value. This model can display the feature of the subconscious mind: the method of human thinking, like the logical mind, is not linear; on the contrary, the mind has an understanding of the whole problem and evolves into a "regional" way; As a result, researchers believe that this would be useful for more development of artificial intelligence. During recent years, the observable Markov decision processes (POMDP) found significant applications in medical decision-making for preventing, screening, and treating diseases. A study by Steimle and Denton (2017) reviewed the models and methods being used for chronic diseases. In this regard, an educational program on developing and solving these significant issues was presented, emphasizing some of the challenges related to chronic diseases including diabetes, heart disease, and cancer. Then, critical considerations indicated two examples of model formulation and solution methods. The first example was an MDP model for the optimal control of addiction treatment decisions to manage the risk of heart disease and stroke among patients with type 2 diabetes. The second example was a POMDP model for optimally designing biomarker-based screening policies for prostate cancer. Such a study ends with a discussion on the challenges of using MDPs and POMDPs in the medical field and explains some significant future directions for research. The Operations Research Interests Group (ORIG) in the medical decision-making society is a multidisciplinary interest group of the professionals being specialized in taking an analytical approach for medical decision-making and medical care. ORIG refers to the use of mathematical methods related to operations research to obtain data-driven solutions to complex health problems and encourage collaboration in some fields. A study by Capan et al. (2017) introduced operations research and drew attention to the opportunities which could be used for facilitating healthcare solutions. Decision making is the process of selecting between possible solutions to a problem based on specific criteria. Depending on the problem, the methods which are part of operations research (e.g., linear programming, Markov decision processes) or the methods which stem from relevant areas (e.g., regression from statistics) can be integrated into the solution approach. This study described the features of the various methods being used for making health decisions. Transplanted patients typically receive high doses of medications as a mechanism for reducing the risk of organ failure. Nevertheless, this method puts them at risk for diabetes after transplantation due to the effect of these medicines. Such a common problem is the imbalance between the risk of not accepting the organs of the body in the face of various factors which create ambiguity in quantifying the risks of wrong positive and negative errors in medical tests, unavoidable estimation errors while using datasets, variety in physicians' attitudes to ambiguous results, and changes depending on patient risk and patient health conditions. In order to address these challenges, Bolori et al. (2020) used a partially observable Markov decision framework (APOMDP) in which dynamic optimization, due to the "cloud" of probable models, allowed decisions to be resilient against risks are. First, various structural results were presented for facilitating the description of the optimal policy.

They compared the optimal policy to the current performance and some other criteria using a set of clinical data and discussed various meanings for both policymakers and physicians. In particular, the results indicated that significant improvements could be achieved in two significant aspects of patients' quality of life expectancy (QALE) and medical costs. Chronic diseases can be decreased or prevented by changing the behavior of patients and physicians. Incentives are one of the mechanisms for stimulating this change. In a study by Drougard et al. (2017), a multi-period random two-player game model was presented where the patients and primary care physicians decided on chronic disease management activities. This model was regarded for patients' decisions in line with primary interaction and lifestyle, as well as physicians' choice to clinical encounters. The behavioral aspects of the patient's decisions were recorded through the health belief model. Patient-physician interaction as a random game - random sum was modeled through the switching control structure. A nonlinear programming (NLP) method was used for finding the optimal strategies for agents. Using data on coronary heart diseases provided a numerical example of how the effects of behavioral barriers and stimuli affected the patients' and physicians' decisions. The results presented some insights for health policymakers on how to design the incentive mechanisms which help manage chronic diseases effectively. Personalized medicine sought to select and modify the treatments based on the patient's characteristics and priorities. A study by Choi et al. (2017) developed an automatic strategy for selecting and modifying blood pressure treatments allowing the patients with various characteristics to use various types of medications and doses and there were various side effects among the patients with such characteristics. In this study, the Markov decision process (MDP) was developed to include meta-analytical data and estimate optimal behavior for maximizing the low-quality life (QALYs) based on the patient's individual traits, using drug adjustment options when the patient was affected by side effects.

A study by Jean-Baptiste and Mihailidis (2017) developed partially observable Markov decision processes where the probability of the transition of the state and measurement are determined with unknown parameters. In this study, a theoretical-data solution method, adaptively managing the exploitation of exploratory trade was suggested. Ultimately, numerical experiments were provided to obtain a guided dose in the healthcare sector.

Previous studies on the dynamics of acute postoperative pain focused on evaluating daily pain but could not evaluate daily changes in the intensity of acute pain. In a study by Tighe et al. (2016), 476107 cases, out of 8346 surgical patients, of acute postoperative pain intensity were studied from day 1 to day 7 using Markov chain modeling to describe the transfer of the patient from one state of pain to another in a probabilistic method. Markov chain is untraceable and positive and can be absorbed without the state. The maximum transfer density was observed in the diagonal area of the transition matrix, indicating that the patients were more likely to be in the same state as the current state. In addition, the probability density would slightly increase if being transferred to sleep or zero state from the current state. The results indicated that the Markov chain is a practical method for describing the probabilistic paths of postoperative pain and pointed to the probability of using the Markov decision process for establishing continuous interactions between pain intensity scores and postoperative labor pain interventions

A study by Zois (2016) studied a review of the models which are expected to be personalized in providing preventive health services along with the relevant solution techniques. A tempting question in medical informatics is how to transfer knowledge from heterogeneous datasets and then to clinical decisions as a generalization. The emergence of large-scale data integration in electronic health records (EHR) offers many opportunities. However, our ability to extract decision support effectively is limited due to the complexity of clinical states, decision-making processes, data loss, and the lack of analytical tools for counseling based on statistical relationships. A study by Tsoukalas et al. (2015) aimed at developing and evaluating a data-driven approach inferring the probability distribution of patients' current status, probable paths,



optimal antibiotic management measures, mortality projection, and life expectancy. The present study presented a framework based on possible data to support the clinical decision in sepsis-related cases. In the beginning, behaviors, observations, and rewards were defined based on clinical performance, specialized knowledge, and then displayed in the EHR dataset of 1492 patients. Then, the partially observable Markov decision process model (POMDP) was used for inferring the patient's optimal line-based policy and evaluating the performance of model-derived policies in a separate test set. Policy decisions focused on the type of antibiotic compounds. Researchers indicated that a data-driven model could suggest desirable measures and project mortality and long-term survival with high accuracy. Such action presents a solid foundation for a scalable clinical decision support framework for sepsis treatment which can be generalized to other relevant clinical cases and practices.

### **3.2. Coronary heart disease screening**

Coronary heart disease is the main cause of death and a major part of healthcare costs in the U.S. and the world. High blood pressure was indicated as a significant risk factor for coronary heart diseases. The author developed data mathematical models for optimizing treatment decisions and supervising blood pressure in order to maximize public health. The first section revealed that the patient's blood pressure record is a critical predictor of coronary heart risk in the future. Standard risk prediction models only regard the patient's current blood pressure and ignore the date. The improved predictability has been indicated using previous blood pressure measurements using the survival analysis of the Cox model and the Framingham heart study dataset.

In the second section, an optimal treatment policy develops the population level. Blood pressure, as a continuous-time and random process in a continuous state, models a geometric composite model of geometric motion indicating a good statistical fit. A closed-form is created for the expectation and variance of a patient's risk during the next three years using the published parameters on the risk of coronary heart diseases as a function of blood pressure. The effects of various doses of anti-hypertension treatment and treatment decisions are optimized using the meta-analysis and analysis of random control trials. In the third section, two identification algorithms are developed for monitoring hypertension and other health technologies that can collect large amounts of traditional clinical measurements. In the first algorithm, the knowledge of disease progression is applied for maintaining a Bayesian idea in the real situation. Such a method is highly accurate while it is difficult to adjust the algorithm in practice because of parameter estimation and simulation requirement. As a result, it develops an unlimited change detection algorithm which is simple and generalizable to other continuous health features including cholesterol, glucose levels, and pulse.

Human beings' reliability and human activities are highly significant to the new complexities of life, work, and medical development (Hagberg et al., 2000). Markov model is a well-defined method for estimating the rate of transmission between the steps of chronic disease. A study by Meenaxi and Singh (2018) focused on analyzing the survival of a patient with chronic heart failure because of reduced destruction fraction. The objective of this study was to describe the progress of chronic heart failure (CHF), estimate the average time spent in each step, and estimate life expectancy. The mean rest time, probability distribution, and the expected number of patients in each case were derived in this study using Kolmogorov's differential equations. There is an increasing consensus that all healthcare costs should be included in economic evaluations for HTAs, especially those associated with long life expectancy. The objective of a study by Lomas et al. (2018) was to quantify the ranging effects of cost categories on deciding on a hypothetical intervention and the uncertainty of this decision for spontaneous coronary artery disease (SCAD) based on a dataset of 94966 patients. Target costing scenarios were considered as the cost of coronary heart disease (CHD), cardiovascular disease (CVD), and all

costs. The first two cases indicate the various interpretations of what may be considered as related costs. The results indicated that cost categories involved the economic evaluation of the effect of SCAD on estimates of cost-effectiveness and uncertainty of decision making.

### **3.3. Cancer and Chronic disease screening**

After the accurate testing and planning of evaluations, the National Cancer Screening Program (CRC) program with the testing of biennial fecal immunochemical tests (FITs) began in the Netherlands in 2014. A national data system was developed for real-time monitoring and timely evaluation. In a study by Toes-Zoutendijk et al. (2017), the data were collected from the first year of this screening program to determine the significance of programming and monitoring the performance of the optimal screening program. The National Screening Information System tracked the number of invitations sent in 2014 as well as FIT kits and colonoscopies. Participation rates were specified by age, the number of positive test results, and positive predictive values (PPV) for advanced neoplasms every week, three months, every year. Finally, it was indicated that the close monitoring of the implementation of the Dutch National Screening Program was allowed to adjust the elimination levels of the program immediately to optimize the performance of the program. China began a breast cancer screening program for women living in rural areas aged 35-64 at a moderate risk in 2009. The program used ultrasound with clinical examination as a primary screening tool. Breast cancer screening was used through ultrasound in 2012 and mammography was performed on the women in the urban areas aged 40-69 being at high risk and identified through a risk assessment questionnaire. The objective of a study by Sano et al. (2018) was to study the effectiveness of breast cancer control in comparison with the lack of screening among the women in the urban and rural areas of China. For this purpose, a Markov model was presented for estimating the cost and effect of life on breast cancer in the urban and rural areas of China. The uncertainty of the parameter was studied using the probabilistic sensitivity analysis. The results indicated that screening for asymptomatic disease in the general population through current screening tools was not cost-effective in a rural environment with a low incidence of breast cancer. In a study by Wu et al. (2018), the severity of breast cancer detection because of screening among the women aged 50-69 was estimated using individual screening data from an organized population screening program in Stockholm Province during 1989-2014. The hidden Markov model was developed with four hidden modes and three observed modes to estimate the normal progress of breast cancer and test sensitivity. The point-to-point transition rate was used for considering the time variable transfer rate. The expected number of cases of non-progressive breast cancer was calculated. The findings indicated that early diagnosis by organized mammography for the women aged 50-69 in Stockholm was a minor phenomenon. The frequency of early diagnosis during the screening was more common than the later periods. The non-homogeneous model worked more effectively compared to the traditional homogeneous model.

A study by Gordon et al. (2018) estimated the costs of the prostate cancer health system with the disease risk group and type of treatment during 2016 - 2025 and identified the potential strategies for curbing the increase of the cost. The cohort model of Markov was created by using clinical methods from the guides of the US prostate cancer and clinical specialty. The estimates of various probabilities of treatment, their results, and unit costs were prepared from regular studies, meta-analyses, epidemiological publications, and national cost reports. Unilateral and probabilistic sensitivity analysis evaluated potential changes in modeled costs. The results indicated that some strategies are critical to diagnosing patients early before the spread of cancer for preventing 42% of growth during the next decade. Increasing the absorption of active monitoring can result in significant cost savings in low-risk prostate cancer management. The circular colon model was used in 2016 to inform the colorectal cancer screening guidelines for information on the Colorectal Cancer Screening Guidelines (CRC) of

the US Preventive Services Force. In a study by Peters et al. (2018), the optimal screening strategies were studied regarding the increased CRC detected among the youth. The authors modified the MISCAN-Colon model for indicating the higher incidence of CRC among the youth who were thought to be at increased risk for cancer.

The obtained life expectancy (LYG; interest), the number of colonoscopies (COL; load), and the useful extra load ratio (productivity ratio  $[ER] = \Delta COL / \Delta LYG$ ) were predicted for various screening strategies. Various strategies vary based on test methods, age of onset (40, 45, and 50 years) and age of screening (75, 80, and 85 years), as well as review intervals (depending on screening methods). The obtained analysis indicated that screening may be performed earlier than previously suggested based on the increased incidence of CRC among the youth. The main goal of Grover et al. (2018) was to study the significance of CA15-3 as an indicator of disease in monitoring and evaluating disease progress among the patients with breast cancer using the multiple Markov model. Based on the marker range, the mode was defined and the transition intensity, transmission probability, and specific survival time of the expected mode were estimated. Furthermore, the effect of age, tumor size, tumor grade, including lymph nodes, ER status, PR status, etc., on transition intensity was studied.

### **3.4. Hepatitis**

Cipriano et al. (2018) identified a random dynamic programming approach for optimal intervention and data collection policies simultaneously. This framework is applied for evaluating the screening of the birth of the hepatitis C virus.

It was emphasized how a time parameter (HCV outbreak) affects the optimal data collection policy for a fixed parameter during the birth of hepatitis group C. The results indicated that delaying data collection can increase efficiency as long as the data sufficiently affect decisions. A dynamic programming framework makes it possible to evaluate the marginal value of data and determine the optimal policy for example when and how much data are collected.

### **3.5. Healthcare management (HCM)**

Onar et al. (2018) reviewed studies on healthcare management (HCM). The results of this review can be classified as follows. The effects on quantitative and qualitative techniques in health management, the effects on case studies of health, and the effects related to health literature reviews. Then, they classified the techniques and approaches applied in healthcare studies and presented some relevant studies under each category. The common goals of the HCM studies in the literature can be classified as the quality of healthcare, performance improvement, patient satisfaction, and financial performance. The review of the literature indicated that quantitative techniques are applied more than qualitative techniques in the HCM. In quantitative techniques, the most common methods are simulation, operations research techniques, statistical analysis, multi-criteria decision-making techniques, and data mining. Arruda et al. (2018) introduced the shortest path algorithm for inferring the optimal disease detection policies for diagnosing the diseases. This algorithm applies a Bayesian method for inferring the probability after the test. Dynamic programming algorithms are applied for finding the optimal sequence of tests for diagnosis. This algorithm presents the shortest random path to find the optimal sequence of tests for approving or disapproving a disease for each specific optimization criterion. The idea is to select the best sequence where a series of tests can be applied with a look at the minimum cost of resources. The proposed approach infers an optimal policy by which the decision-maker is provided with a test strategy for every previous probability of disease to achieve the subsequent probabilities which guarantee the immediate treatment or incorrect diagnosis.

On the other hand, some research studies have been done to deal with the scheduling of medical staff at hospitals considering mathematical programming and solution algorithms. Cissé et al.

(2017) conducted a review research on the home health care routing and scheduling problem (HHCSP). Another review work was performed by Fikar and Hirsch (2017) on the HHCSP. They highlighted the recent advances on the topic and discussed future research directions. Marynissen and Demeulemeester (2019) reviewed recent research works conducted on the multi-appointment scheduling problems at hospitals. They evaluated the main limitations, challenges and opportunities for future research directions.

### **3.6. Limited optimization methods in healthcare**

Currently, limited optimization methods are widely applied in healthcare for solving problems like traditional applications of operations research methods such as selecting an optimal location for new facilities or creating the most efficient operating room capacity. In a study by Crown et al. (2018), the application of these methods to find optimal solutions to problems in providing health services and related policies was evaluated. For this purpose, three award-winning studies on healthcare delivery or policy development reflecting an optimization algorithm were selected. Two out of three studies were reviewed using The Professional Society for Health Economics and Outcomes Research (ISPOR) being provided from the framework presented in the human resources report of the initial optimization. The first case study indicated the application of linear programming for determining the optimal combination of screening and vaccination strategies to prevent cervical cancer. The second case revealed the application of the Markov decision process to find the optimal strategy for the treatment of type 2 diabetes for hypercholesterolemia using statins. The third study was used as an educational tool and its goal was to describe the characteristics of a radiation therapy optimization problem and invite the reader to form a mathematical model for solving the problem. This example is highly interesting because it addresses an extensive range of possible models including linear, nonlinear, and mixed-integer programming formulations.

The conclusion expresses the limited optimization methods in presenting feedbacks to decision-makers on the favorable solution solutions and the rate of loss, profit, or increased costs related to the final clinical decision or selection of related policies. The failed identification of a mathematical or optimal solution indicated a missed opportunity for improving economic efficiency in healthcare delivery and clinical results of patients. Such a report indicated the relationships of finite optimization methods to the economic modeling of a simple formula and identified some of the major types of finite optimization models including linear programming, dynamic programming, numerical programming, and random programming. The second report showed the use of limited optimization methods in healthcare decisions using three case studies which focused on the determination of screening and vaccination strategies for cervical cancer, the timely onset of statins in diabetes, and educational record for encouraging readers to form the problems of radiation therapy optimization. Such factors indicate a wide range of problems which can be limited by optimization methods.

### **3.7. Machine intelligence algorithms in healthcare**

Today, the US healthcare industry can only save \$300 per year using machine data for analyzing a rich set of available medical data; The results of these analyses can lead to the progress like more accurate medical diagnosis, the discovery of new treatments for diseases, and cost savings in the process of patient admission to healthcare organizations. Since healthcare applications are inherently related to the large amounts of data, it is highly useful to run any algorithm on medical data. The significant signs of progress that were made in computing power during the past decade provided an opportunity for many researchers to implement various health care applications which have not been effectively implemented on previous computational platforms. Shishvan et al. (2018) studied machine intelligence

algorithms within the framework of healthcare applications; a survey including a comprehensive list of computational models and computational algorithms. The application of this algorithm has been indicated in a few steps, i.e., data acquisition, feature extraction, and aggregation, modeling, algorithm training, algorithm implementation, and detailed presentation, as well as case studies for each step. A set of criteria was used for evaluating the modeling and performance of the algorithm facilitating the comparison of the proposed models and algorithms.

### **3.8. Cyber-physical in healthcare**

Cyber-physical systems were provided as an emerging case study of machine intelligence in healthcare. The authors concluded their study by providing a list of opportunities and challenges to involve machine data into health care programs and provide a comprehensive list of tools and databases to contribute to other researchers. The targeted classification of sound signals can make considerable progress in screening the structural disorders of the heart. In a study by Alexander et al. (2018), an algorithm was suggested based on auditory filter models and probabilistic division of cardiac cycle sequences for classifying phonocardiogram signals (PCG) as normal or abnormal.

First, it includes the division of heart recordings into a sequence of four steps of the heart, i.e. S1, systole, S2, and diastole using the hidden Markov model. Second, using the gammatone filter model, the features of the gammatone frequency cepstral coefficient (GFCC) are divided into two categories of independent binary classification problems: one with PCG decomposition and the other one without classification. The proposed algorithm indicates a strong and acceptable performance for automatic screening of heart sound signals and can be a useful diagnostic tool in clinical practice for indicating structural and functional heart diseases.

### **3.9. Artificial intelligence and Machine learning in healthcare**

The uses of artificial intelligence in medicine are being turned into a hot topic in health data systems with the development of machine learning techniques. In a study by Yuan et al. (2017), a new basic heart failure database was provided including 1715 patients and 400 features. Then, a new machine learning method called support vector machine was proposed to help physicians diagnose heart disease. After being solved by this method, the algorithm parameters were obtained which could be used for determining the patient's heart disease status. In order to solve the problem of database dimensions and increase the speed of the model, the PCA, L-DA, CCA, and LPP methods were used for reducing the features. Ultimately, the performance of the method was compared with A Library for Support Vector Machines (LibSVM) and elm and then the effectiveness of this method was indicated experimentally by comparing its performance to LibSVM and elm.

**Table 1. Investigation of the most relevant research papers in the literature**

References	Objective	Methodology	Approach			
			Model Presentation	Analytical	Dynamic System	Uncertainty
Güneş and Örmeci (2018)	Application of operations research in different aspects of disease screening	Microsimulation models, Compartmental models, general stochastic models, and partial MDP		*		
Petousis et al. (2018)	Using reversal learning to create reward commitments for Markov decision protocol of lung and breast cancer screening	Markov decision approach and the maximum entropy approach to the reversal learning algorithm	*			
Wu et al. (2018)	Evaluation of active classification of dynamic systems with a finite set of MDP models	MDP and system dynamics	*		*	
Dai and Tayur (2018)	Estimation of optimal blood pressure treatment policies	MDP and Poisson regression	*			
Denton (2018)	Introducing some of the most commonly used methods for creating and solving models for optimizing sequential decision making in early diagnosis of diseases	MDPs, partially observed MDP, and data-based operations research methods		*		*
Bonifonte (2018)	Development of analytical tools using operational research and statistical methods to solve problems in cardiovascular disease and blood pressure management	Unlimited change detection algorithm, Bayesian and meta-analysis of experiments, randomized control	*			
Onar et al. (2018)	Review articles on health management, review of objectives and techniques used	Analytical evaluation		*		
Aroda et al. (2018)	Optimal policies for diagnosis of diseases	The shortest path algorithm using the Bayesian method	*		*	
Cipriano et al. (2018)	Simultaneous identification of optimal intervention and data collection policies	Stochastic dynamic programming			*	
Crown et al. (2018)	Evaluation of the application of limited optimization methods to find desirable solutions for problems in health care provision and related policies	Analytical evaluation		*		
Hudson (2019)	Selection of breast cancer screening method under uncertainty	MDP and Perseus algorithm	*			*
Yaylali and Karamustafa (2019)	The impact of obesity on cancer and the risks of mortality	MDP	*			
Hynninen et al. (2019)	Optimizing population-level utilization and targeting genetic tests alongside traditional risk factors in prevention from cardiovascular events	Decision-making/analytical model		*		
Latha and Vetrivelan (2019)	Prediction of cardiovascular disease modeled using a partially observed MDP	Partially observed MDP	*			
Belciug and Gorunescu (2020)	Describe the advantages of smart decision support systems in medical research	Intelligent decision support systems and machine learning techniques		*		

#### **4. Conclusion and suggestions for future studies**

A brief review of operations research (OR) applications on the healthcare system was addressed in this paper. The purpose of this paper was to identify the existing literature on the wide range of operations research (OR) studies applied to healthcare and to classify studies based on application type and disease on the OR technique employed. Based on this review, we recognized that commonly used OR approaches fall into four categories: mathematical programming, heuristics, and simulation.

The progress in vaccines, development of hospitals, new medicines, and therapies preventing the death of children, developed medical equipment, etc. have been the measures taken for improving the health system indicators in all centuries. Nowadays, the use of operations research, in various fields involving health is expanding which, as a quantitative systemic method, can significantly solve the problems associated with the health system. In this study, these methods were compared based on a table after evaluating the use of operations research models based on research processes in health systems, including Markov decision processes (MDPs) and partially observable Markov decision processes (POMDP) based on the research process in health systems. The base of this study was evaluating the publication of scientific studies on operations research topics in the health systems.

The Internet of Things (IoT) and its infrastructure has the potential for revolutionizing healthcare (Liu et al., 2015). Network body measurement tools, with the sensors in our living environment, enable a real and continuous collection of data about our physical and mental health. Such data should be effectively used so that they can be used in treatments. However, a lot of medical decisions in nature are consecutive and unsustainable. Sequential decision-making models, including Markov decision processes (MDPs) and partially Markov decision processes (POMDP) are powerful tools for modeling and solving such random and dynamic problems.

The Internet of Things and its infrastructure, which is a new topic, have the potential of revolutionizing healthcare. Network body measurement tools, with the sensors in our living environment, enable a real and continuous collection of data related to our physical and mental health. Such data should be effectively applied so that they can be used in treatments. Researchers are expected to evaluate the health system on the Internet of Things, review some techniques for solving the related problems, and describe a range of health applications using these tools since the various challenges and opportunities arising in implementing smart health care services are highlighted.

Considerably less work appears to have been carried out with potentially promising methodologies such as scenario planning, robust optimization, and reliability modeling. In particular, adaptability and reliability aspects are important for healthcare delivery systems to perform well despite capacity limitations or facility closures (Daskin and Dean, 2004). Tackling the wide range of optimization problems in healthcare will certainly require a considerable amount of research work. Identifying the optimization issues and capturing relevant parameters in mathematical models can be challenging. Finding appropriate solution techniques or formulating new methodologies for solving the models can be tricky. Although OR researchers have already dealt with many new problems and solution methodologies, much remains to be investigated and solved in this enormous as well as complex problem domain.

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