TECHNICAL MEMORANDUM

DATA MINING APPLICATIONS IN MEDICAL INFORMATICS

Prepared By

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SUMMARY

The large increase in the amount of medical data becoming available is making it necessary to provide physicians and public health authorities with intelligent assistance in the decision making process. Conventional statistical methods have long been used in medicine, but modern machine learning approaches; e.g. neural networks, can handle a large number of input variables, require less user intervention and are better in handling nonlinearities and in dealing with data uncertainties and inaccuracies. This Technical Memorandum proposes the use of abductive networks machine learning as a data mining tool for performing modeling, analysis, and classification tasks in medical informatics. Applications include the classification and diagnosis of diseases, selection of optimum treatment methods and intervention courses, and automated biochemical analysis. Compared to neural networks, the proposed abductive networks technique offers a number of advantages, including simplified and more automated model synthesis requiring less user intervention, and analytical input-output model relationships that automatically highlight significant input parameters and provide better explanation capabilities.

The proposed work should be of interest to medical and health care concerns in the Kingdom (both academics and practitioners) who need to apply modern data mining techniques for discovering underlying relationships in medical surveys and for developing low-cost screening tools to assist in diagnosis. Other applications include prognosis and risk assessment studies as well as the development of intelligent tools for computerized training of medical and nursing students. Benefits include better understanding of epidemiological factors, easier and more accurate disease diagnosis and classification, and improved utilization of human and other health care resources.

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SECTION 1 INTRODUCTION

Medicine has always benefited from technological advances. Modern developments in computers, lasers, ultrasonic imaging, etc. have boosted medicine to extraordinary levels of achievement. Advances in computing and communications have culminated in the new field of medical informatics that deals with the storage, retrieval, sharing, and optimal use of huge amounts of biomedical data, information, and knowledge. A prime concern in medical informatics has been to derive useful information from the large amounts of data available for problem solving and decision-making. In the medical practice there is always a need to classify patients, screen high-risk population, predict disease stage, categorize data into various groups, prognosticate, and choose best treatment options. Traditionally statistical models are used to solve such problems. However, due to inherent noise and wide variability in medical data, use of pre-defined model structures, and invalid pre-assumptions of linearity, the statistical models fall short of desired accuracy in many situations. There is an increasing awareness that the knowledge base of biomedicine is essentially unmanageable by traditional methods, and that the process of informed decision making is as important to modern biomedicine as is the collection of data on which clinical decisions or research plans are made.

Data mining and intelligent data analysis techniques offer a new approach to handle this information overload. They automatically discover patterns in medical data to provide support for the decision-making process in many health care areas, including screening, diagnosis, prognosis, monitoring, therapy, survival analysis, and hospital management. Data mining functions include classification, association detection, sequential/temporal pattern detection, and clustering/segmentation. Tools used for performing such functions include: Bayesian and nearest-neighbor classifiers, rule induction methods, decision trees, genetic algorithms, fuzzy logic, and artificial neural networks (ANN). The latter machine learning tool has been used in various medical applications, including diagnostic systems, biochemical analysis, and image analysis in many areas such as cardiology, neurology, psychology, oncology, radiology, neurosurgery, genetics and urology. However, neural networks suffer from a number of limitations, e.g. long training times, difficulties in determining optimum network topology, and the black box nature with poor explanation facilities. Here we propose using the alternative abductive networks approach that avoids such limitations for solving problems and developing applications that are of interest to both researchers and practitioners in the health care sector of the kingdom.

SECTION 2 OBJECTIVES

We propose to apply the abductive network data-based modeling approach to the important area of data mining of medical data collected by hospitals and healthcare authorities in the kingdom. Resulting applications will serve the following objectives:

- Improve our understanding of public health issues and the ways in which new knowledge can be derived from medical health surveys.

- Improve the management and utilization of health care resources through segmentation of patient population, forecasting of patient volume, predicting inpatient length of stay, etc.

- Optimize the use of expensive and scarce health care facilities through the development of effective and low-cost screening tools.
- Improve health care in clinical settings through the use of fast, computerized diagnostic aides that handle a large number of inputs simultaneously without being affected by fatigue, working conditions, emotional state, or habituation.
- Facilitate new discoveries through the interpretation of complex data being generated in the basic biomedical sciences.
- Develop training tools for use in medical and nursing colleges.

SECTION 3 DISCUSSION OF THE PROBLEM

3.1. Description of the Problem

While it took 150 years for the amount of information in the world to double in the year 1900, this is now happening every few months. Health care generates mountains of administrative data on patients, hospitals, bed costs, as well as medical data in the form of health surveys, clinical trials, electronic patient records, and computer-supported disease management. The sheer volume of the data makes it difficult for conventional data analysis methods such as plotting and manual inspection of correlations to extract useful information for decision support. Data mining techniques are becoming indispensable in discovering patterns and relationships hidden in the databases and allowing health care professionals to integrate them into the decision making process.

Physicians are trained to make diagnostic judgments by aggregating many types of clinical data. However, recent years have witnessed a dramatic increase in disease markers that a doctor can rely on [1]. With data warehousing and general-purpose, wide-range data collection being introduced in hospitals, hundreds of data items will be available in each medical record. It is well established that humans can not analyze such complex data in an ad hoc manner without errors [2], and there is a growing need for computerized techniques that perform the fusion of a large number of acquired data parameters to assist physicians in taking the right decisions. Basic data analysis tools based on descriptive statistics included hypothesis testing and simple linear regression [3]. For a few parameters, multiple linear regression analysis was used [4], but it is difficult to determine regression equations that adequately model complex and nonlinear relationships. Also, the user imposes a given form of the model relationship that may not be the most appropriate one.

A recent trend in handling such difficult problems has been to resort to artificial intelligence and machine learning data mining techniques. The techniques range from knowledge-based approaches in the form of expert systems to data-driven methods such as rule induction, regression trees, genetic algorithms, and neural networks. Although rule-based medical expert systems, e.g. [5], have been developed, the technique has proved of limited use due to the difficulty in elucidating knowledge from the domain experts and the poor definition of factors that influence diagnosis by physicians [1]. Data-based modeling techniques are non-parametric, i.e. the user does not have to explicitly specify the model design. This enhances their use in knowledge discovery by freeing them from being biased or influenced by previous assumptions.

With this approach, a model for the phenomenon considered is automatically developed through supervised training on a database of solved examples. Once synthesized, the model can be used to perform fast predictions of outputs corresponding to new cases; previously unseen during training. Data-based modeling offers a number of advantages over conventional modeling approaches, including increased tolerance to noise, reduced need for knowledge on the modeled phenomenon, the relative ease of updating the model through re-training, and the fact that no programming is involved as models are synthesized automatically. In the last few years, neural networks have been applied to a wide range of medical applications leading to improved diagnosis and prognosis through automatic analysis of data [2].

3.3. Proposed Approach

In spite of the wide-spread use of neural networks as a modeling tool, the technique suffers from a number of limitations, including long training times and the difficulty in determining optimum network topology and training parameters, the over-fitting problem, and the black box nature and the associated lack of explanation facility which does not appeal to physicians [2]. For medical data mining applications, we propose using abductive networks [6] as an alternative machine learning approach to overcome such limitations. Compared to neural networks, the method offers the advantages of faster training and more automated and faster model development requiring little or no user intervention [6]. With the resulting model represented as a hierarchy of polynomial expressions, derived analytical relationships can be compared with previously used empirical or statistical models to gain better insight into the modeled phenomena. The technique automatically avoids over-fitting through using a criterion for penalizing complexity [6], without requiring a dedicated validation data set; thus leaving more training data for use in actual model synthesis. The approach has been successfully used at KFUPM in a variety of medical informatics applications which are reviewed in Section 5.

A database consisting of an adequate number of solved examples is required to develop and evaluate the abductive network model. The dataset should include input variables that are likely to influence the output parameter to be modeled, as well as corresponding values of the output parameters as determined by other elaborate tests or expert opinion. The model synthesized through training on the dataset is then evaluated on a subset of the data reserved for this purpose and not used previously during training. The model is validated through examining its performance on this evaluation data set. The proven model can then be put to actual use for predicting process output and can be integrated in the client's medical informatics system. Work on the project involves coordination with the client in identifying a suitable application area, preparing the required databases, performing data pre-processing to ensure good quality of the training and evaluation data, as well as in model integration. Model performance will be analyzed and compared with that of existing models and diagnosis methods.

SECTION 4 STATEMENT OF WORK

The proposed work includes the following tasks:

4.1. Problem Identification

Identify a suitable application area of interest to the client. Depending on the application, it may be adequate to use already existing historical input-output data for building and evaluating the required model. Task 4.2 is required only if this is not the case and the data need to be collected especially for the project.

Data-based modeling techniques have been used in a wide range of data mining applications in medicine. Following is a brief outline of the areas covered with only a few examples of each. The review is meant to serve only as a guide for possible applications that may be of interest to the client.

a. Screening Tools

Improved public awareness of health risks has increased the demand on health care resources at primary care centers, clinics and hospitals. Rigorous examination for clinical diagnosis often requires the use of costly and scarce facilities and manpower. In many cases, it turns out that the tests were not necessary. For example, a sleep study using nocturnal polysomnography (PSG) is currently the diagnostic standard for the sleep apnea (SA). However, the technique is costly, inconvenient to patients, and may not be readily available in many locations. It has also been observed that with PSG performed on all patients having symptoms of the syndrome, only 70% of these patients were found to have SA [7]. Therefore a considerable number of patients undergo unnecessary and expensive tests; thus increasing health care costs. Well-validated simpler clinical screening or case-finding tools could reduce the number of such sleep investigations by as much as 30% [7]. Data-based modeling techniques have been used to build screening tools for the early detection of prostate cancer based on blood tests of PSA [8], breast cancer [9], heart diseases [10], diabetes [11], and hepatitis [12]. Doyle et. al. compare standard screening methods, statistical models, and neural networks for the screening of hepatoma in cirrhotics during liver transplant evaluation [13]. Models use historical data on previously diagnosed cases to relate the presence of the disease to patient's data, health parameters that are readily available or easy to measure, and response to self-reporting questionnaires.

b. Diagnostic and Classification Systems:

Computer aided diagnostic systems offer significant potential for providing accurate and automated diagnostic technology that assist the physician in handling the large number of parameters in modern clinical settings, particular in stressful situations as in intensive care units (ICUs). These tools are also better-placed than humans for dealing with typical shortcomings of medical data, including incompleteness and uncertainty. Studies have been reported for the diagnosis/classification of eye diseases [14], glaucoma [15], diabetic retinopathy [16], aphasia [17], toxocariasis [18], leukemia [19], and pigmented skin lesions [20]. Other examples include classifying patients in the otherwise poorly defined area of rheumatic disorders [21], classification of chest pain symptoms [22], predicting the risk of coronary artery disease from information on the serum lipid profile [23], early diagnosis of heart attacks in patients admitted to emergency units [24], and detection of hepatoma in patients with cirrhosis based on information collected at the time of evaluating a liver transplant [25].

Some systems rely for the diagnosis on the automated analysis of medical physiological signals in the form of time series, such as the ECG signal for arrhythmia classification [26], the EEG for discriminating between dyslexic subtypes [27] and the classification of sleep stages [28], as well as EMG diagnostics [29]. Schemes have been reported for the detection of myocardial ischemia through the analysis of the ST-T complex of the ECG signal [30] and the evaluation of muscle diseases through the analysis of magnetic resonance spectroscopy data [31].

Systems have also been developed for the analysis of medical images from a variety of imaging modalities. Applications in this area include the automatic detection and classification of micro-calcifications in mammograms [32] and in ultra-sonograms [33], classification of chest x-rays, classification of tissues and vessels in magnetic resonance images (MRI), x-ray spectral reconstruction, determination of skeletal age from x-ray images, and determination of brain maturation. Neural networks models were used for the detection of the coronary artery disease through the automatic processing of single photon emission computed tomography (SPECT) images [34]. They have also been used to classify Pet scans of normal and alzheimer-disease subject [35], pancreatic masses based on CT findings [36], and diabetic maculopathy through automated analysis of color retinal images [37].

c. Therapeutic Aides:

Computational intelligence tools can also assist in the treatment of patients through helping the clinician select the most appropriate course of intervention based on the effectiveness of alternative treatment methods, as modeled using available historical data. Neural network models were used for evaluating treatment plans for radiotherapy [38,39] and for assisting with decision making for the management of patients in ICUs [40]. Other systems predict appropriate medication doses; e.g. for the management of diabetic patients. One such system [41] simulates the patient’s blood glucose profile for the next day and suggests required insulin dosage accordingly. Recent neural networks applications include predicting transfusion requirements for ER patients [42].

d. Prognosis

Accurate prognosis and risk assessment are critical for the improvement of disease management and outcome. Models were developed for performing survival analysis for AIDS patients [43], risk stratification in heart failure [44], and breast cancer prognosis [45]. Systems have been proposed for predicting pre-term birth risk [46], ambulation following spinal cord injury [47], and death and myocardial infarction following coronary angioplasty and stenting [48]. Other applications include assessing survival after colon carcinoma [49] and ovarian carcinoma [50] treatments, evaluating complications of kidney transplantation [51], estimating the probability of survival after trauma [52], determining cardiac surgical risk [53], prognosis of the femoral neck fracture recovery [54], and predicting outcome of treatment in ICUs [55].

e. Biochemical/biological Analysis:

Intelligent data analysis systems have been used to automate a wide variety of analytical tasks, e.g. analyze blood and urine samples, track glucose levels in diabetics, determine ion levels in body fluids, and detect pathological conditions such as tuberculosis [56], for determining enzymatic glucose by flow injection analysis [57] and discovering alarm rules for validating microbiological data [58]. Schweiger et al. [59] compare the performance of neural networks and conventional statistical methods for the evaluation of laboratory data.

f. Hospital Management

Computational intelligence models can perform many forecasting and prediction functions that assist in the efficient running of a hospital complex through optimizing the utilization of facilities and allocation of resources. For example, neural network models have been used to predict the length of stay (LOS) for incoming psychiatric patients requiring hospitalization [60]. Such systems can achieves considerable savings by determining which patients would benefit most from short stays and which require long-term hospitalization. Forecasting of patient volume [61] and ambulance run volume [62] can also help streamline operation, optimize utilization of resources, and plan future expansion.

g. Epidemiological Studies

Data-based modeling techniques are well-suited to study the distribution and determinants of health and diseases, morbidity, injuries, and mortality in human communities. Epidemiology can benefit considerably from data mining tools in looking for patterns relating outcomes to exposure to potential causal or risk factors. Neural networks were used to detect excess deaths due to cholera [63], study soybean rust epidemics [64], model the epidemiology of schistosomiasis-mansoni [65], and assess asthma strategies in inner-city children [66]. Abductive network models can help in disease explanation by automatically identifying the most influential determinants, and can even provide an analytical relationship for the outcome parameter in terms of such factors.

h. Training of Medical Students

Models developed for various diseases or groups of diseases can be useful in training undergraduate students in medical and nursing schools; e.g. [67]. Neural networks and other machine learning techniques have proved useful in developing intelligent tutoring systems for assisting in teaching the decision-making process in medical education [68]. The student can use the model to interactively explore the effect of various disease markers on the outcome and to check if he/she can make correct diagnosis. Such models have been proposed for assessing medical students problem solving performances on computer-based simulations [69]. Abductive network models can be easily integrated into user-friendly graphic interfaces using popular programming platforms such as Visual Basic or LabVIEW.

4.2. Data Collection

Data for model synthesis and evaluation are often taken from available historical databases or may need to be collected especially within the framework of a particular investigation. To obtain good models, the training set should be a good representation of the problem space. The learning task is simplified by utilizing domain expert knowledge on parameters relevant to the model in the choice of input variables to be included in the training database. This reduces training time and leads to simpler and more accurate models.

4.3. Data Preprocessing

Data gathered shall be examined to check for completeness and avoid obvious errors. Missing data values could be estimated by interpolation, or the whole data row is discarded. Obvious outliers should be removed and data are usually normalized as Z scores of zero mean and unity standard deviation by subtracting the column mean and dividing by the column standard deviation. The opposite operation restores the model output to the original problem space.

4.4. Model Development

Records constituting about 70% of the total data are randomly selected for use in synthesizing an abductive network model that describes the input-output relationship. A model is synthesized for each variable declared as ‘output’. The remaining 30% would be reserved for model evaluation.

Abductive network models take the form of layered feed-forward networks of functional elements (nodes) [6]; see Figure 1. Elements in the first layer operate on various combinations of the independent input variables (x's) and the single element in the final layer produces the predicted output for the dependent variable y. Both the element type and the combination of inputs to it from all previous layers are selected automatically for best prediction performance. Networks are limited to four layers, and training is stopped automatically at a point in time that strikes a balance between model complexity (which ensures adequate learning of the training data set) and model simplicity (which results in better generalization in predicting new cases when the model is put to actual use). Neural networks usually use a separate validation dataset to prevent over-learning, which reduces the number of cases available for actual training.

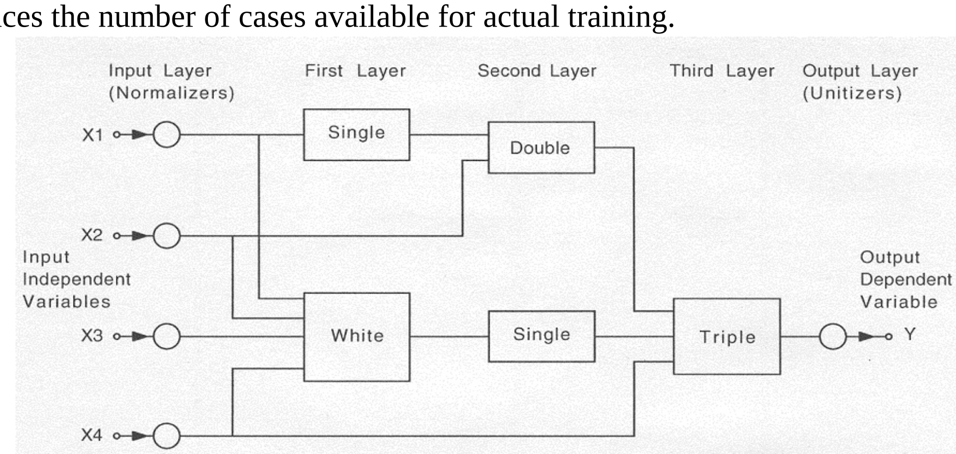

Figure 1. A typical abductive network model showing various types of functional elements

The following main functional elements are supported:

(i) A white element consisting of a constant plus the linear weighted sum of all outputs of the previous layer, i.e.:

"White" Output $= w_0 + w_1x_1 + w_2x_2 + w_3x_3 + ... + w_nx_n$

where $x_1, x_2, ..., x_n$ are the inputs to the element and $w_0, w_1, ..., w_n$ are the element weights.

(ii) Single, double, and triple elements implementing a 3rd-degree polynomial expression with all possible cross-terms for one, two, and three inputs, respectively; for example,

"Double" Output $= w_0 + w_1x_1 + w_2x_2 + w_3x_1^2 + w_4x_2^2 + w_5x_1x_2 + w_6x_1^3 + w_7x_2^3$

This allows taking into account nonlinear combinations of the input variables automatically as required. Substituting the equations of the functional elements of the various layers gives a polynomial expression relating the modeled output to the input variables.

4.5. Model Evaluation and Analysis

The resulting model is evaluated on the evaluation set of the database, previously unseen during training. Various procedures for error analysis will be employed. In addition to predicting the modeled output from measured inputs, the resulting abductive network model provides useful information on the modeled relationships. The model automatically selects input parameters that contribute most to the modeled output and can provide simplified analytical expressions for the model relationship that reveal significant input variables and their relative importance. These expressions can be easily imported to other analysis/visualization software packages. With neural networks, this information can only be derived through the inspection of large weight matrices. Derived model relationships will be compared with any empirical or regression analysis relationships that may exist for the phenomenon being modeled.

4.6. Model Integration

The resulting model is ported onto the computer system at the client site. Depending on the application, the model may be integrated to operate with other software programs and database applications. In situations where inputs to the model include patient data acquired online, the model should be interfaced to the software that controls the measurement apparatus. This part of the work requires close cooperation with engineers and technicians at the client's site.

4.7. Performance Assessment

Evaluate the performance of the model in realistic operational settings for extended duration. Study the level of acceptance of the new model by the client's work team. Solicit and implement recommendations from the client team for product improvement. Investigate the need for model updating to accommodate long-term drifts in training data.

4.8. Documentation

Full documentation will be provided on the data sets used, pre-processing employed, model synthesis, resulting model structures and input-output relationships, model evaluation analysis, and model integration.

SECTION 5 RELEVANT EXPERIENCE AT CCCR

CCCR has the resources and expertise to develop data mining solutions for the modeling and analysis of medical data. CCCR researchers have previously collaborated with faculty members of the medical schools at King Saud University, Riyadh, King Faisal University, Dammam, Cairo University, Egypt, for the development of a number applications in medical informatics. Following is a brief description of some applications:

5.1. Modeling Obesity Using Abductive Networks [70]

Obesity, as represented by the waist-to-hip ratio (WHR) risk factor, was modeled using 13 other health parameters. Models trained using 800 cases predict the WHR as a continuous parameter with errors below 7.5% for 90% of another set of 300 evaluation cases. Categorical models predict correct logical WHR values in 99.3 % of the evaluation cases. Analytical relationships derived for simplified models confirm the strong correlation between WHR and diastolic blood pressure, cholesterol level, and family history of obesity.

5.2. Modeling and Predicting the Educational Score in School Health Surveys with Abductive Networks [71]

The educational score in a health survey of 2720 primary school children was modeled in terms of the child's age, gender, vision, nourishment, parasite infection, family size, and parents' education. Models synthesized using only 100 randomly selected cases predict the educational score for all the remaining cases with 100% accuracy. Simplified analytical models provided useful insights into the influence of parameters such as father's education and the number of children in the family.

5.3. Classification of Urinary Stones by Cluster Analysis of Ionic Composition Data [72]

Cluster analysis was used to classify a set of 214 kidney stones based on data of nine chemical analysis parameters. The set was previously classified empirically into three stone classes based on percentage concentrations of the urate, oxalate, and phosphate radicals. The study investigated the effect of utilizing all the nine chemical parameters for the classification and compared the performance of various clustering techniques, distance and similarity measures, and data standardization methods. Cluster analysis could match the empirical analysis with only 6% error. Carbon ions alone provided a single classifier for the three stone categories with a matching error of about 10%.

5.4. Modeling and Forecasting Patient Volume at a Primary Health Care Clinic Using Univariate Time-Series Analysis [73]

Univariate time-series analysis was used to model and forecast the monthly patient volume at a primary health care clinic. Based on nine years of data, an ARIMA model forecasts data for the following two years with an average and maximum absolute errors of 1.86% and 4.23%, respectively. Another approach that extrapolates the growth curve of annual means using a polynomial fit gives the better figures of 0.55% and 1.17%, respectively.

5.5. Improving the Classification Accuracy of Medical Data Using Network Committees (Ensembles) [74, 75]

We explored ways of using abductive network committees (ensembles) for improving classification accuracy in medical diagnosis. Using 2 or 3-member committees with member networks trained on different subsets of the training data achieved up to 5 percentage points improvement in the classification accuracy over the best single model using the full training set for the Pima Indians Diabetes, Heart Disease, and the Dermatology standard datasets [74]. Similar improvements were obtained by training the members on mutually exclusive subsets of the input features ensuring that members have approximately equal predictive power [75]. Feature grouping in this way was performed using a novel GMDH-based feature ranking approach [76].

5.6. Improving the Classification Accuracy of Medical Data Thorough data Reduction [76]

Complete feature ranking followed by selection of the optimum subset of input features has lead to 54% reduction in data dimensionality for the Heart Disease dataset, with significant improvements in the classifiers performance and implementation. Ranking was performed using properties unique to GMDH-based learning algorithms [76]. Reducing the number of attributes to be measured for model implementation makes screening tests faster, more convenient and less costly. Simpler models with fewer inputs are also more transparent and more comprehensible, providing better explanation and justification for the suggested diagnosis.

5.7. Improving the Classification Accuracy of Medical Data Thorough Problem Decomposition [77]

We have investigated improvements gained by problem decomposition for the classification of the 6-class Dermatology dataset. Two-stage classification schemes based on hierarchical decomposition of the diagnosis problem boosted the classification accuracy from 91% for the single-classifier monolithic approach to 99%. Such models are also simpler, achieving up to 47% reduction in the number of input features used, thus reducing the cost and improving the convenience of performing the medical diagnostic tests required. Automatic selection of only relevant inputs by the simpler abductive network models synthesized provides greater insight into the diagnosis problem and the diagnostic value of various disease markers. The problem decomposition approach helps plan more efficient diagnostic tests and provides improved support for the decision making process.

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