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Use of Fuzzy Logic Based Decision Support Systems in Medicine

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ABSTRACT The complexity of the problems that are faced within people's decision-making process can reveal a variety of challenges in the solution process. The increasing complexity of the events faced, makes the decision-making more difficult. Therefore, recently, a trend has occurred in advanced technologies such as decision support systems (DSS). DSS offer alternative solutions with a flexible and objective perspective to researchers in various fields, particularly in the fields of medicine and life science. DSS can be designed using artificial intelligence based methods such as fuzzy logic (FL), and artificial neural networks (ANN). Nowadays, the fuzzy logic-based DSS in the medical field such as the disease diagnosis, the determination of appropriate treatment, the costs and so on, including issues in making clinical decisions are widely used, and successfully applied. In this study, FL-based DSS have been introduced, and different applications used in the medicine field have been given. The mean of the success level of the FL-based DSS was determined to be ninety percent. FL-based DSS has been providing a significant contribution to disease diagnosis in the examined studies.

INTRODUCTION

People encounter different problems throughout their lives, and they are required to make the right decisions for the resolution of these problems both quickly and accurately. People should behave in a rational and objective manner when making these decisions. However, it is difficult to correct and impartial decision-making can move away from the optimal solution because of people's emotional differences, experiences, and values judgments. Especially in health and life sciences, making the right decisions is of vital importance most of the time. Possible errors could affect the quality of people's lives. Therefore, to reduce the margin of error to a minimum or not to make mistakes, all alternatives should be evaluated in an impartial manner at the optimal time period in the decision-making process.

Due to the developments in the IT technologies, diagnosis, treatment of illnesses and patient pursuit are effected by those developments as well at the medicine field. However, due to the usage of IT technologies on medicine field, it is open for failure of complexity and uncertainty according to the used systems such as FL, ANN and genetic algorithm (Adeli and Neshat 2010). FL is a method that is based on artificial intelligence. FL is used to represent mathematical modeling of the knowledge and linguistic variables. Thus, it has provided that computers can solve the problems similar to human experts (Samuel et al. 2013). FL provides a means for dealing with imprecision, vagueness and uncertainties in health data (Ekong et al. 2012; Vaghela et al. 2015). FL-based DSS are very powerful tools for data and knowledge management for clinical studies (Belard et al. 2016). Today's technology allows the design of a DSS that helps people make accurate, fast, and economical decisions in problem solving. In an uncertain environment, the DSS created using FL is one of the artificial intelligence based methods that is quite successful in the processing of linguistic data. The problems that are encountered in daily life include a vast majority of uncertainties, which are quite difficult to solve with mathematical models are dominated by the Aristotelian logic. Disease's diagnosis consists of couple levels of uncertainty and imprecision. For instance, it is only given per two different situations for logical values of black-white and true-false, 1-0.

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Fig 1. Clinical decision support system with fuzzy logic. *Source:* Authors

Nonetheless, in reality it is not that simple. The real life is not only black and white, but most of the time, it is like a spectrum of rainbow colors. Therefore, for more realistic results, it is safe to consider moderate logical values. Nowadays, uncertainty is considered a core concept for both FL and science that needs to be dealt with natural language (Saleh et al. 2011; Chen and Bau 2013; Fraccaro 2015).

The aim of the study is to assist in the successful and accurate execution and in decisionmaking and knowledge management in the DSS developed for use in the field of health. Therefore, in this study, FL-based DSS was introduced and examples were presented from the successful applications in the health.

MATERIALAND METHODS

In this study, the basic information regarding FL-based DSS and examples of studies in medicine was presented. Important databases such as Elsevier, Wiley and Springer, were scanned in the research process. The selected search criteria were determined as "FL", "Diagnosis with FL", "DSS in medicine" and so on.

Fuzzy systems are one of the most active research fields in recent years because it has

many benefits in solving complicated non-linear system modeling. Fuzzy systems' most important advantages are the simplicity for the obvious knowledge representation in the form of if-then rules, a mechanism of reasoning in human understandable terms, the capacity of taking linguistic information from human experts and combining it with numerical information, and the capability of approximating complex non-linear functions with simple models. Unlike classic modeling, where a single model is used to describe the global behavior of a system, fuzzy rule-based modeling is essentially a multi-model approach in which individual rules are combined to describe the global behavior of the system Soria et al. (2013). The overview of clinical DSS with FL is located in Figure 1. As shown in Figure 1. basically the operation of clinical DSS begins with planning, and the next step is pre-processing of data. Data pre-processing can be done through some multivariate statistical analysis such as factor analysis and PCA. Data is processed in DSS and a system decision (disease diagnosis) is obtained.

The operation diagram of FL-based DSS is located in Figure 2. First of all, researchers are required to plan their research and move in this direction expediently, as in many statistical anal-



Source: Authors

ysis methods. Accurately and reliably obtained data in accordance with research subjects directly affects the accuracy of the analysis and the quality of research. The data analyzed in the FL-based DSS in the medical field may have the various parameters associated with the diseases, disease inputs and patient information (age, gender, chest pain, heart rate, blood pressure). This condition may change according to the model the researchers will perform. Fuzzy systems are knowledge-based systems that are configured using FL theory. FL-based DSS basically consists of three components. These are fuzzification, fuzzy inference engine and defuzzification.

The fuzzification is the first stage of the fuzzy system operation. There are two meanings of fuzzification. The first meaning is that it is converted into a fuzzy degree of a membership value expressed by an absolute value and the second is that it is the process of converting a linguistic variable with a certain degree of membership using the appropriate membership function from an input value. There are different membership functions used in fuzzification stage, as seen in Figure 2. For this purpose, the membership functions to be used at this stage and these functions' position in the x-axis and number (subset number) are determined. Although there are a large number of membership functions, in the fuzzification stage, the most widely used are triangular, trapezoidal, and Gaussian functions (Wang 1997; Akkaptan 2012). Besides, there are membership functions more practically unused such as sigmoidal, S and Pi (Đ). The membership function is a function indicating the degree of fuzzy sets in possession of an object, and allows the calculation of the membership value of $\mu_A(\chi)$. It is the membership function of the fuzzy set. This function, which receives the value of the x elements, is called the membership values in the fuzzy set. It is shown in the form of $\mu_A(\chi) \rightarrow [0, 1]$. The formulation of the membership function is indicated as triangular in Equation 1, trapezoidal membership function in Equation 2, and gaussian membership function in Equation 3, respectively.

$$\mu_A(x; a, b, c) = \begin{cases} a \le x \le b & (x-a)/(b-a) \\ b \le x \le c & (c-x)/(c-b) \\ x > c \text{ or } x < a & 0 \end{cases}$$
[1]

$$\mu_A(x; a, b, c, d) = \begin{cases} a \le x \le b & (x-a)/(b-a) \\ b \le x \le c & 1 \\ c \le x \le d & (d-x)/(d-c) \\ x > d \text{ and } x < a & 0 \end{cases}$$
[2]

$$\mu_A(x;m,\sigma) = exp\left[-\frac{1}{2}(\frac{x-m}{\sigma})^2\right]$$
[3]

It is located at the base of fuzzy rules inference engine with the inference unit. Here, the data is processed by the 'if-then' rules. The learning process takes place here in the FL.

Expert opinions, specific results on diseases elements can be represented by the rule base. Thus, the aim of preventing human errors arising from emotional and biased perspective. Information regarding the input variable values are processed and converted into the fuzzy value and obtaining new information provided. Information is modeled in different ways in the inference unit. Different inference methods can be used in this stage, as seen in Figure 2. These are the Mamdani, Larsen, Tsukamoto, and Tagaki-Sugeno-Kang (Dubois and Prade 1980; Klir and Yuan 1995). In Mamdani inference method, the result fuzzy set is created on the basis of the union operation in the fuzzy sets and defuzzification process must be carried out. Mamdani inference method's rule structure is as follows.

If
$$x_1 = A_1$$
 and $x_2 = B_1$ Then $z_1 = C_1$
If $x_1 = A_2$ or $x_2 = B_2$ Then $z_2 = C_2$ [4]

If Blood Pressures is Normal and Heart Rate is Normal Then The Status is Normal

(Dutta et al. 2013).

Larsen method works with product operation and defuzzification process must be carried out too. The rule structure of the Takagi-Sugeno-Kang inference method is indicated in Equation 5. Output variable is not a fuzzy set, instead it is a crisp value or a linear function in Takagi-Sugeno-Kang method. In this regard, there is no need for defuzzification.

If
$$x_1 = A_1$$
 and $x_2 = B_1$ Then $z_1 = f(x_1, x_2)$

If
$$x_1 = A_2$$
 and $x_2 = B_2$ Then $z_2 = f(x_1, x_2)$
or

If
$$x_1 = A_1$$
 and $x_2 = B_1$ *Then* $z_1 = C_1$

If
$$x_1 = A_2$$
 and $x_2 = B_2$ Then $z_2 = C_2$ [5]

(Sivanandam et al. 2007).

Each consecutive fuzzy rule is showed by fuzzy sets with a monotonically membership function in Tsukamoto inference method. The output fuzzy set is a set of elements represented by a monotonic membership function.

The values obtained from the fuzzy inference mechanism were converted into the absolute value defuzzification unit. The most encountered defuzzification methods in the literature are the Maximum Membership Principle Method, the Centroid Method, the Mean of the Maximum Membership, the Weighted Average Method, the Smallest of Maximum Method, and Largest of the Maximum Method Ross (2004). Output variable represents the system decision on defuzzification formulas. In the medical field, the system decision may indicate the existence of disease or a rating that indicate the various levels of the disease.

RESULTS

Research results reveal detail in the overall situation of FL-based DSS and other systems working with in diagnosing disease. The use of FL-based DSS on health systems has become more important over recent years. The researchers examined 71 FL-based DSS studies in medicine conducted between 1997 and 2016. Details of these studies were given in Table 1. FL-based DSS were used in almost all medical fields. But it was usually used to calculate the risk in cancer patients and diagnosis of heart disease. Studies more diagnostic, disease classification and risk calculation was conducted.

FL based DSS seems to be used more intensively in the diagnosis of heart diseases and cancer, as shown in Table 1. The distribution of cancer types is given in Figure 3. Breast cancer among cancers is the most studied type of cancer as shown in Figure 3.

The numbers of input variables used in examined publication are seen to be varying from three to thirty-seven. Excess in the number of input variables provided that diseases can be examined in detail and are versatile. The inclusion of input that known effect on the output to model is very important. However, keeping the optimal number of inputs is vital in terms of time and cost savings and system processing. In order for this, an adequate infrastructure, technical personnel, and the obtained data should be managed correctly. Nonetheless, the operation of system may slow down and may occur as a complex structure with the increase of the rule number. This is partly associated with quality of used software and computer hardware. The number of variables that vary according to the structure of the problems can be resized at the ideal level that is subjected to pre-processing. For this, multivariate statistical methods such as factor analysis and PCA can be used.

A large part of the parameters used in the articles that listed in Table 1 consists of measured values related to disease. In addition to this, it is observed that researchers also benefit from visual and sensory materials such as ultrasound images and EEG-ECG signals. It is seen that the output of designed system in the articles is in the form of generally diagnose, graded levels of disease and different classes or levels of risk. In the scope of study, the parameters used in the literature where the applications for the breast cancer is as follows, that is, contour, density, distribution, clump thickness, uniformity of cell size, uniformity of cell shape, marginal adhesion, single epithelial cell size, bare nuclei, bland chromatin, normal nucleoli, area, perimeter, texture, radius, smoothness, concave points, symmetry, uniformity, homogeneity, age, age at



Fig. 3. Type of cancers *Source:* Authors

Year of publication	Paper title	Authors	Year of publication	Paper title	Author
1997	Entropy Measure of Fuzziness in the Detection of QRS Complex in a Noisy ECG scimol	Czogala et al.	2012	Decision Support Systems in Medicine - Anaesthesia, Critical Care And Intensive Care	Hemmerling et al.
1997	A Decision-Driven Design of a Decision Support System Anesthesia.	Graaf et al.	2012	A Belief Rule-Based Decision Support System for Clinical Risk Assessment of Cardiac	Kong et al.
1997	Fuzzy logic based decision support system	Khamseh GM	2012	Clinical Decision Support System for Dental Treatmont	Mago et al.
1997	In partonogy Automatic Detection of Cardiac Contours on MR Ymages Using Fuzzy Logic And Dynamic Procramming	Lalande et al.	2012	Diagnosis of Arthritis through the Fuzzy Inference System.	Singh et al.
2001	Fuzzy Logic For Decision Support in Chronic Care.	Beliakov and Warren	2012	Fuzzy Method for Pre-diagnosis of Breast Cancer from the Fine Needle Aspirate Analysis	Sizilio et al.
2003	A Fuzzy Expert System Design For Diagnosis of Prostate Cancer	Saritas et al.	2012	Diagnostics Decision Support System for Tuberculosis Using Fuzzy Logic	Soundararajan et al.
2005	Genso-FDSS: A Neural-Fuzzy Decision Support System for Pediatric ALL Cancer Subtype Identification Using Gene Expression Data	Tung and Quek	2012	Fuzzy Modeling and Control of HIV Infection.	Zarei et al.
2006	A Fuzzy Rule-Based Decision Support System for Duodopa Treatment in Parkinson	Ahmed et al.	2013	Clinical Decision Support System for Diagnosis of Pneumonia in Children.	Adewunmi and Adekunle
2006	An Example of the Determination of Medicine Dose in the Treatment bythe Fuzzy Method	Allahverdi et al.	2013	Fuzzy Logic Based Anaesthesia Monitoring Systems for the Detection of Absolute Hydroxolaemia	Baig et al.
2006	Neuro-Fuzzy System for Prostate Cancer Diagnosis.	Benecchi L	2013	Support System for Decision-making in the Identification of Risk for Body Dysmorphic Disorder: A Fuzzy Model	Brito et al.
2006	Diagnosis of Heart Disease using Artificial Immune Recognition System and Fuzzy Weighted Pre-Processing	Polat et al.	2013	Fuzzy Expert System for Predicting the Pathological Stage of Prostate Cancer.	Castanho et al.
2006	Applying Fuzzy Logic and Network to Rheumatism Treatment in Oriental Medicine	Thang et al.	2013	Design of Fuzzy Classifier for Diabetes Disease using Modified Artificial Bee Colony Alcorrithm	Beloufa and Chikh
2006	An Application of Takagi-Sugeno Fuzzy System to The Classification of Cancer Patients Based on Elemental Contents in Serum Samples.	Zhang et al.	2013	A Novel Fuzzy Expert System for the Identification of Severity of Carpal Tunnel Syndrome.	Kunhimangalam et al.

Table 1: Fuzzy logic based decision support systems studies in medicine

DECISION MAKING PROCESS IN MEDICINE

Table 1: Co	ontd				
Year of publication	Paper title	Authors	Year of publication	Paper title	Author
2007	A Hybrid Approach to Medical Decision Support Systems: Combining Feature Selection, Fuzzy Weighted Pre-Processing and AIRS	Polat and Gunes	2013	Decision Support System for Asthma (DSSA).	Mishra et al.
2007	Fuzzy Expert System for Fluid Manage- ment in General Anaesthesia.	Rahim et al.	2013	Fuzzy Analysis of Breast Cancer Disease using Fuzzy C-Means and Pattern Reconstition	Muhic I
2008	An intelligent system based on fuzzy probabilities for medical diagnosis – a study in aphasia diagnosis	Moshtagh- Khorasani et al.	2013	A Web-based Decision Support System Driven by Fuzzy Logic for the Diagnosis of Typhoid Fever	Samuel et al.
2008	An Adaptive Fuzzy Logic Based Diagnostic Decision Support System for Critical Care Medicine.	Liyanage et al.	2013	A Quantifier-Based Fuzzy Classification System for Breast Cancer Patients	Soria et al.
2008	Ovarian Cancer Diagnosis with Complementary Learning Fuzzy Neural Network	Tan et al.	2014	Medical Diagnosis System using Fuzzy Logic.	Awotunde et al.
2009	A concernent of the second sec	Begum et al.	2014	Neuro-Fuzzy Methodology for Diagnosis of Autism.	Ahuja and Kaur
2009	A Hybrid Hierarchical Decision Support System for Cardiac Surgical Intensive Care Patients. Part I: Physiological Modelling and Decision Support System Design	Denai et al.	2014	Simulation of Medical Diagnosis System for Malaria Using Fuzzy Logic.	Jimoh et al.
2010	A Fuzzy Expert Systemfor Heart Disease Diagnosis.	Adeli and Neshat	2014	Automatic Classification of Epilepsy Types Using Ontology-based and Genetics-based Machine Learning.	Kassahun et al.
2010	Evaluation of Breast Cancer Risk By Using Fuzzy Logic.	Caramihai et al.	2014	Fuzzy Logic System For Risk-Level Classification of Diabetic Nephropathy	Narasimhan and Malathi
2011	An Experimental Comparison of Fuzzy Logic And Analytic Hierarchy Process for Medical Decision Sunnort Systems	Uzoka et al.	2014	Clinical Decision Support System for Diagnosing Heart Disease.	Suchithra and Maheswari
2011	Building Interpretable Fuzzy Models for High Dimensional Data Analysis in Cancer Diagnosis.	Wang and Palade	2015	Development of a Fuzzy Decision Support System to Determine the Severity of Obstructive Pulmonary in Chemical Initiaed Victims	Samad-Soltani et al.
2011	Evaluation of Breast Cancer Risk By Using Fuzzy Logic.	Balanica et al.	2015	A Fuzzy Logic Decision Support System for Assessing Clinical Nutritional Risk.	Hadianfard et al.
2011	A Decision Support System for Tuberculosis Diagnosis.	Djam and Kimbi	2015	A Fuzzy Logic Model for Differential Diagnosis of Lower Urinary Tractdysfunctions.	Lopes et al.

Table 1: Contd...

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Year of publication	Paper title	Authors	Year of publication	Paper title	Author
2011	A Fuzzy Expert System for the Manage-	Djam et al.	2015	Clinical Decision Support System based on	Douali et al.
2011	Decision Support System for the Intelligent Identification of Alzheimer's using Neuro	Obi and Imainvan	2015	ruzzy cognuve maps. Computer-aided Diagnosis System Based on Fuzzy Logic for Breast Cancer	Miranda et al.
2011	r uzzy togue. A Decision Support System Model for Diagnosing Tropical Diseases using Fuzzy Logie.	Olabiyisi et al.	2016	Categorization. Decision Support System for Fatty Liver Disease Using GIST Descriptors Extracted from Ultrasound Images.	Acharya et al.
2011	Decision Support System for the Diagnosis of Asthma Severity Using	Patel et al.	2016	Developing a Fuzzy Expert System to Predict	Safdari et al.
2011	Skin Cancer Recognition by using A Neuro-Fuzzy System.	Salah et al.	2016	Development of a Clinical Decision Support System for Antibiotic Management in a	Canovas-Seura et al.
2011	A Fuzzy Decision Support System For Management of Breast Cancer.	Saleh et al.	2016	Evaluation of Predictive Machine Learning Techniques as Expert Systems in Medical	Godara and Singh
2011	An evolutionary-fuzzy DSS for assessing health status in multiple sclerosis disease	Esposito et al.	2016	Diagnosis. Fuzzy Risk Assessment of Mortality after Coronary Surgery Using Combination of Adaptive Neuro-fuzzy Inference System	Nouei et al.
2012	Clinical Decision Support System: Risk Level Prediction of Heart Disease using	Anooj PK	2016	and K-means Clustering. Mortality Prediction of Septic Shock Patients Using Probabilistic Fuzzy systems.	Fialho et al.
2012	weigned ruzzy rules. Fuzzy Logic Based Smart Anaesthesia Monitoring System in the Operation	Baig et al.	2016	Predicting Recycling Behaviour: Comparison of a Linear Regression Model and a Fuzzy	Vesely et al.
2012	I nearre. Intelligent Decision Support System for Depression Diagnosis Based on Neuro- fuzzy-CBR Hybrid.	Ekong et al.		Logic Model.	

Table 1: Contd...

first menstruation, number of invaded axillary nodes, bi-rads score, estrogen receptor, progesterone receptor, c-erbB2 (HER2), cytokeratin 5/ 6, cytokeratin 7/8, EGFR, c-erbB3, c-erbB4, p53,

6, cytokeratin 7/8, EGFR, c-erbB3, c-erbB4, p53, Mucin1, number of invaded axillary nodes, tumor surface, grade, hormone receptor, lymph node, and tumor size. The variables used in the study of prostate cancer are age, tPSA, fPSA, percent fPSA, PSA density, and transition zone PSA density. In a study of skin cancer variables used are irregularity index, percent asymmetry, red color variance, green color variance, blue color variance, red relative chromaticity, green relative chromaticity, blue relative chromaticity, spherical color coordinates (1), spherical color coordinates, color coordinates, red ratio, green ratio, blue ratio, difference in lightness, difference in chroma, and difference in color. The outputs of designed system in cancer studies are cancer risk level, disease diagnosis and classification.

Inputs used in the cardiology are age, gender, chest pain, resting blood pressure, serum cholesterol, fasting blood sugar, resting electrocardiographic results, maximum heart rate achieved, exercise induced angina, old peak, depression induced by exercise relative to rest, the slope of the peak exercise, segment, number of major vessels colored by flourosopy, weight, cholesterol and thallium scan. Outputs in this field are chest pain risk status, mortality and heart disease level.

Sample sizes in most of the examined studies are comparable suitable for DSS, which is created with the help of FL. It can be noticed that success rates of the designed systems are at quite high levels. It has been shown that it is been utilized from accuracy, sensitivity and efficiency criteria as well as Roc Curve in order to evaluate system performance. The success level of the fuzzy systems in examined articles was determined at an average level of ninety percent. In a number of studies, systems are also included that it is been integrated computer systems with different working and artificial intelligence methods. Fuzzy systems are quite successful applications, which located in the various automation systems that developed by the authors or within the hospital are quite successful applications.

DISCUSSION

DSS are powerful software tool for medical studies to assist health workers in the decision-

making process. Especially, organizational and diagnostic issues are under study of DSS. Due to the kind of inputs, DSS can provide advisory decision in form of monitor alerts, color codes, or visual messages. DSS has been improved for increasing the quality of care (Hemmerling et al. 2012). FL-based DSS have widespread use in the field of health sciences. It provides great benefits to researchers and health professionals particularly for diagnosing illnesses, management services, laboratory services, and various issues related to patients, with functions such as image and signal processing (Czogala et al. 1997), monitoring and control (Mahfouf et al. (001), forecasting, clustering (Acton et al. 1999; Arifet al. 2010) and classification (Narasimhan and Malathi 2014). In this study, a comprehensive and updated review of the literature was aimed at and useful results were obtained.

It is seen that providing information from experts for the creating rule base of FL based DSS, as shown in Table 1. At this point, the most important source of information is physicians. Benefiting from a large number physician specialists in their field of knowledge and experience is very important either creation of the ifthen rule or comparative evaluation of system results. Some studies in the literature, system decisions are compared with independent decision of a large number specialist doctors in the same field. Consistent and successful results were obtained. This situation reveals that the FL based DSS in the field of medicine are a very powerful decision tool.

The number of variables that are used in examined publication is quite high compared to other studies in the field of life sciences. Incomplete assessments can lead to negative consequences in the health field. In addition, another important factor is the number of cases in the interpretation of system performance. Specifically, it is necessary to work with high success rates and a large number of cases in the analysis of serious diseases such as cancer, to be considered successful systems analysis. In this study, it was determined that the number of cases is at quite a reasonable level in research on cancer (Benecchi 2006; Muhic et al. 2013; Soria et al. 2013; Godara and Singh 2016).

Considering the high rate of success in the literature, providing a significant contribution to physicians and healthcare organizations such as support disease diagnosis, treatment options,

prevention of medical errors, the creation of nurses to assistance systems, healthcare services, prescription writing and producing the pharmaceutical composition.

CONCLUSION

In recent years, it has been seen that the intensity of efforts to detect serious diseases such as cancer diagnosis and treatment at compiled studies. In addition, as well as the use of computer programs FL, it has also been observed that the development of custom software systems is often used in hospitals. With FL-based DSS, the quality of health organizations plays an important role in improving indirectly. Thanks to its contributions to the development of the process of diagnosis and treatment of diseases, it offers a multidimensional perspective and provides a substantial reduction of costs. Knowledge and experience of medical experts, patient information and inference information based on generated if-then rules located in FL-based DSS. The possibility of evaluation from different angles at the same time can be provided in solving the examined problems. In this study, it is intended to be a source of information in the decision-making process concerning issues such as the identification of disease, the rapid and processing of medical data in a healthy way and the design of an intelligent patient monitoring system for the researchers of the future who will work on FL and a DSS.

RECOMMENDATIONS

In the future, it is expected that there will be developments in health services through the support of artificial intelligence methods such as FL in automation system tools. Thus, FLbased DSS will help healthcare personnel especially in rural areas.

NOTE

This study was presented at the 36th Annual Conference of the International Society for Clinical Biostatics, Utrecht, the Netherlands, August 23 to 28, 2015. Only the abstract of the presentation was published in abstract book.

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