Jimma University

Jimma Institute of Technology

School of Graduate Studies

School of Biomedical Engineering

Bioinstrumentation Chair

Fuzzy and Rule-based Hybrid Expert System for Accurate Diagnosis of Tuberculosis

By: - Meron Aseffa Hailu

A Thesis Submitted to School of Graduate Studies of Jimma University, in Partial Fulfilment for the Degree of Master of Science in Biomedical (Bio instrumentation) Engineering.

September 2020

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Advisors: - Main Advisor – Dr. Kinde Anlay

Co. Advisor – Dr. Bheema L.

September 2020

Jimma, Ethiopia

DECLARATION

I, Meron Aseffa, declare that this research titled, **"Fuzzy and rule-based hybrid expert system for accurate diagnosis of Tuberculosis"** is my original work and has not previously been submitted for a degree or any other qualification at this University or any other institution.

Meron Aseffa Hailu Signature _____ Date 01/10/2020

On behalf of the School of Biomedical Engineering at Jimma Institute of Technology, we the advisors of this research with the title of **"Fuzzy and rule-based hybrid expert system for accurate diagnosis of Tuberculosis"** and we, the evaluators, confirm that this research is approved as MSc. thesis for the student.

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ABSTRACT

Starting from many decades back till recent years, there have been diseases which affect and cause numerous deaths in the human race. Among the deadliest diseases known to man, tuberculosis (TB) is one with a very high mortality rate. One third of the world's population is affected by the disease. TB is one of the top ten deadliest diseases in Ethiopia having the fourth place next to HIV. Poverty, malnutrition, over-crowded living conditions and high prevalence of HIV infection, which are indicators of low and middle income countries like Ethiopia, are some of the risk factors which increase the transmission level.

In the current manual diagnosis of TB, misdiagnosis and diagnostic delays are being witnessed. This is mainly due to TB having different classifications, its nature of mimicking other diseases and the disproportionate number of human TB experts and patients. Even though there are expert systems designed in foreign countries, their questionable accuracy, high technology as well as knowledge requirements and resourceful settings makes them unfit and inapplicable for developing countries.

The objective of the current thesis is to design a diagnostic decision support system for accurate diagnosis of tuberculosis by using fuzzy and rule based hybrid expert systems. Patient diagnosis data was collected from eighty patients, from which seventy five percent of the data was used to formulate the rules used in the system. By using the fuzzy expert system, the patients' symptom severity range was analysed to indicate the suspicion level of each disease. In the fuzzy expert system, fuzzification of the crisp input was made by using triangular membership function and mamdani fuzzy inference mechanism was applied to map the given input variable to an output space. The center of gravity defuzzification method was used in the inference process to obtain a crisp final output for each disease's level of suspicion. Once the disease with the highest suspicion level was found, different examinations were conducted to confirm the suspicion and the findings were analysed by using rule based expert system. In the rule based expert system, by using TB experts' knowledge, rules were formulated and forward chaining inference strategy was applied to reach at a diagnostic conclusion. Among the examination modalities that are used to diagnose pulmonary TB, the chest X-ray classification is made by the system. To design the classification model, two chest X-ray image datasets were used. Data augmentation was applied on the training data to increase the number and variation of data. The model was trained with ResNet50, a pre-trained convolutional network using 80% of the data.

The model was found to have 84% classification accuracy. An interactive user interface was also designed by using visual studio which will make the system more user-friendly. A computerized patient data recording system which will facilitate TB patient follow-up, keep their data safe and make it easily accessible was also incorporated. The database is designed using SQL server.

Finally, after conducting a performance evaluation on the designed fuzzy and rule based hybrid expert system, the system achieved an accuracy of 93%. This result suggests the success of the expert system in increasing the accuracy of tuberculosis disease diagnosis in the absence of human TB experts.

Keywords: Decision support system, Expert system, Tuberculosis

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ACRONYM

AI	Artificial Intelligence
ANN	Artificial Neural Network
CNN	Convolutional Neural Network
COG	Center Of Gravity
COPD	Chronic Obstructive Pulmonary Disease
CXR	Chest X-Ray
DL	Deep Learning
EPTB	Extra-Pulmonary Tuberculosis
ESR	Erythrocyte Sedimentation Rate
FDC	Fixed-Dose Combinations
FIS	Fuzzy Inference Systems
FNA	Fine Needle Aspiration
GIT TB	Gastrointestinal Tract Tuberculosis
GP	General Practitioners
HIV	Human Immunodeficiency Virus
ID	Identification
MDR TB	Multi Drug Resistant Tuberculosis
MS SQL	Microsoft Structured Query Language
MS VS	Microsoft Visual Studio
OPD	Outpatient Department
PTB	Pulmonary Tuberculosis
RESNET	Residual Networks
SGD	Stochastic Gradient Decent
SPSS	Statistical Package For The Social Sciences
SVM	Support Vector Machine
TB	Tuberculosis
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infection
WHO	World Health Organization

ORGANIZATION OF THE THESIS

The thesis consists of six chapters. In the first chapter, overall introduction to the study which includes brief explanation of tuberculosis and its different classifications, components of fuzzy and rule based expert systems, image classification techniques, statement of the problem, significance and objectives as well as scope of the research will be discussed. In the second chapter, different literatures in relation to fuzzy and rule based TB diagnostic expert systems will be reviewed. Chapter three, which is the main part of the thesis, will discuss the methodologies and materials used in order to design the decision support system. In chapter four, the data acquired from the questionnaire and forms will be analysed. In chapter five, the results found during testing the designed system will be discussed. The final chapter concludes and summarizes the research.

DEFINITION OF TERMS

- Human experts - an individual who has a superior capability and understanding of a given problem.
- Image classification - a supervised learning problem which defines a set of target classes and trains a model to recognize them using labelled examples.
- Expert system - a piece of software which uses databases of expert knowledge to offer advice or make decisions in areas such as medical diagnosis
- Decision support system - a computerized program used to support determinations, judgments, and courses of action
- Caregivers - nurses with special training of a specific field to closely monitor patients in need of assistance and care.

CHAPTER ONE

Introduction

1.1 Background

Lower respiratory tract infections (LRTI) are infections in the airways, lungs or below the voice box. Infections in the lower respiratory tract are primarily the result of viruses, bacteria, fungal infections, and mycoplasma. These include influenza or the flu, pneumonia, bronchitis, and tuberculosis [1].

LRTI remained the most deadly communicable disease, causing 3.0 million deaths worldwide in 2016 [2]. In the following year of 2017, LRTIs were considered as the fourth causes of death in the world causing 2.56 million deaths [3]. In the 2019 world health statistics overview of the world health organization (WHO), lower respiratory infections were also considered as the causes of death that most contribute to differences in life expectancy between men and women among other diseases [4]. In Africa, lower respiratory infections are among the deadliest diseases causing around one million deaths each year [5]. Lower respiratory infections are the third causes of death in Ethiopia [6]. Among the lower respiratory infections, tuberculosis is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS) worldwide [7].

1.2 Tuberculosis

Tuberculosis (TB) is a bacterial infectious disease whose etiologic agent is a bacterium called mycobacterium tuberculosis. It spreads by aerosols which are disseminated upon coughing and sneezing. TB causes serious morbidity and mortality by damaging the lungs and other organs [8].

Tuberculosis is one of the top 10 causes of death worldwide [9]. In 2013 tuberculosis was listed as the eighth deadliest infectious disease in the world [10]. In the year 2014, tuberculosis was the second deadliest contagious disease by death toll having 1.3 million deaths [11]. In 2015, there were 10.4 million TB incidents from which 1 million were children. From those total cases, 1.8 million deaths were encountered and 170,000 of those who died were children. In the same year, from recorded HIV deaths, 35% were due to TB, making it the most common cause of mortality among HIV positive people [9]. From the list of top 10 deadly diseases known to man in 2017, tuberculosis was placed tenth [12].

TB statistics in Ethiopia shows that among the top ten causes of death, TB is at fourth place [13]. Twenty two countries, among which Ethiopia is one, were referred as TB "high burden" countries at a global level since 2000 by the WHO [14]. In the same year, "with reference to National Institute for Health and Clinical Excellency recommendations, countries with an estimated incidence rate of 40 per 100,000 or greater are considered to have a high incidence of TB" [15]. Ethiopia is among these countries with incident rate of 207 per 100,000 [15]. In 2016 Ethiopia was still among the 22 "high burden" countries with 219,186 incident of TB cases and 48,910 mortalities [16].

Clinical manifestation of TB

TB bacilli may spread from the initial location in the lungs to other parts of the body via the blood stream, lymphatic system, airways or by direct extension to other organs. Based on this, TB is broadly classified into two: pulmonary TB and extra-pulmonary TB [17].

Pulmonary TB – is a major type of TB which accounts for 65-85% of all TB cases [17].

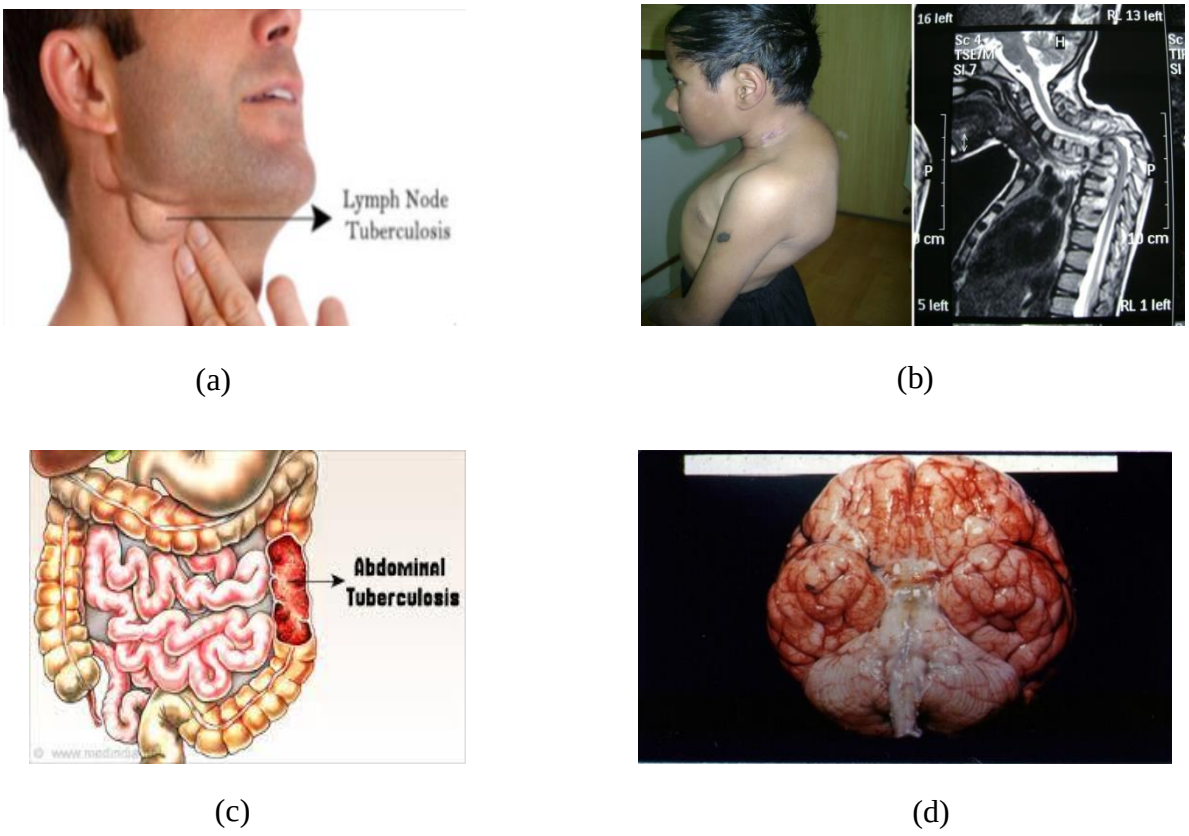
Pulmonary tuberculosis (PTB) is a disease that occurs when the lungs are infected by mycobacterium tuberculosis. The bacilli are disseminated as droplets through coughing or sneezing. If these droplets find a way into another person's body, the fate of the bacilli depends on these three conditions [18]:

- If the immunity of the body is in good condition, it fights and kills the bacteria, "thus preventing the infection" [18].
- The immunity of the body is able to desist the bacteria from causing disease, but not completely destroying it. "This is called **Latent TB**." This form of PTB exists in one thirds of the world's population [18].
- If the immunity of the body is in poor condition due to different reasons, the bacteria assumes control and gets well established in the body. "This is called **Active TB**." In some cases, the latent form of TB can progress to active TB due to changes in the condition of the body's immunity [18].

Common symptoms of active lung TB are cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats. These symptoms vary for different classifications of TB [9].

Extra-pulmonary TB – is another form of TB which occurs when mycobacterium tuberculosis infects different parts of the body other than the lungs [19].

Worldwide, it is estimated that between 10 to 25% of TB infections occur extra-pulmonary, outside of the lungs [8]. TB can affect any part of the body; skin, eyes, heart, arteries, and genital system. The most common forms of extra-pulmonary TB includes: lymph node TB, TB of meninges, TB of the nervous system, TB of bone and joints, and abdominal TB [19]. Images of some of the types of extra-pulmonary TB are shown in figure 1.



(a) (b)

(c) (d)

Figure 1: Major types of extra-pulmonary TB (a) TB of lymph node [20], (b) TB of spinal cord [21], (c) abdominal TB [20] and (d) TB of meninges [22].

1.2.1 TB diagnosis

To prevent the propagation of TB among the society, timely diagnosis is very crucial. The diagnosis of TB is done by inspection from a combination symptoms, clinical signs and investigations. The examination modalities used in the diagnosis of TB majorly include radiologic examinations, AFB smear microscopy and culture and molecular tests [23], [24].

Radiologic examinations

For the diagnosis of active pulmonary TB, chest X-ray is the commonly used radiologic examination. In some cases of pulmonary TB and in extra-pulmonary TB, computed tomography and magnetic resonance imaging (MRI) might also be helpful to achieve correct diagnosis [23], [24].

Chest X-ray has been a part of TB diagnosis for over a century. Chest X-ray is a very helpful tool in the diagnosis, management and follow-up of PTB, especially for patients that are unable to give sputum sample or who have negative smears. Chest computed tomography (CT) is another important radiologic examination tool which is used to evaluate complications that are difficult to detect by using chest X-ray [23], [24].

Acid-fast bacilli (AFB) smear microscopy and culture

Smear microscopy of sputum is a highly specific laboratory examination in the diagnosis of PTB. Because of its variable sensitivity and inability to identify drug-resistant strains, culture confirmation is required whenever possible. Sputum culture, besides from its long time taking process (4-8 weeks in solid medium and 10-14 days in liquid medium) which could delay appropriate treatment, is very sensitive in identifying the bacteria and is crucial for drug susceptibility testing (DST) [23], [24].

Molecular tests

Among the commonly known molecular tests for TB, nucleic acid amplification test, line probe assay and Xpert MTB/RIF are the major ones [23], [24].

Nucleic acid amplification (NAA) test is a very specific laboratory examination and was found to be much faster when compared with sputum culture. The test can be done on a direct clinical specimen; sputum, cerebrospinal fluid (CSF), lymph node aspirates etc… The other molecular test for the diagnosis of TB is line probe assay (LPA). LPA is a highly sensitive and specific test for rapid diagnosis of MTB and DST. It allows specific gene markers to be detected by extracting DNA, performing amplification, hybridization and finally evaluation. The third molecular test is Xpert MTB/RIF or most commonly known as geneXpert. It is a test that is most frequently used due to its ability to detect the specific TB bacteria from different specimen (unlike most molecular tests) and identify rifampicin resistance from sputum within 2 hours of sample collection [23], [24].

From the above stated examination modalities, the most widely used ones in almost all health facilities in Ethiopia as first stand examination for TB are: chest X-ray as a radiologic examination, and geneXpert due to its sensitivity, specificity and availability. The manual diagnosis procedure for TB is shown in figure 2.

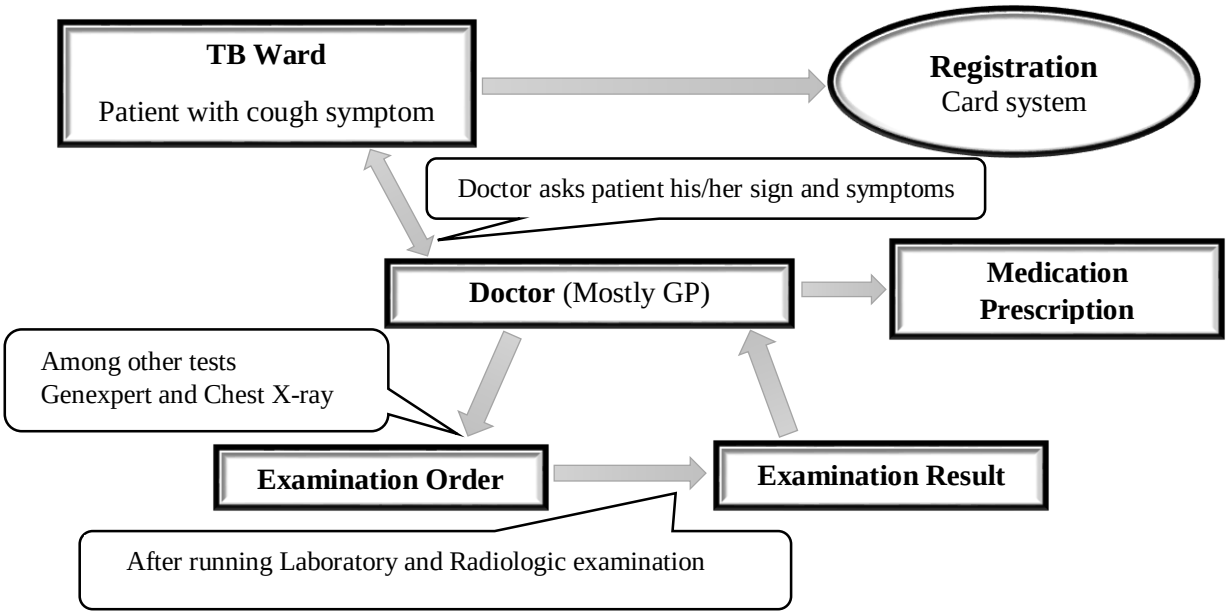


Figure 2: Manual diagnosis procedure of TB.

Late Diagnosis of TB increases the transmission and mortality rate of the disease among the society and in health care facilities [25]. Creating awareness among the society about the disease, the necessity of going to health facility for timely diagnosis when certain indicative symptoms are felt, how it can be treated and that the treatment is given free of any cost is very important. On the other hand, making sure of the availability of well-educated and experienced medical personnel to provide the correct diagnosis and treatment once a patient manages to go to the health facilities is very crucial. The unproportionate ratio of experienced human experts in the field of TB diagnosis to the large number of patients makes it difficult to give the required quality health care service.

As mentioned earlier, TB can affect any part of the body other than its most common site of infection, which is the lung. Pulmonary TB is associated with the convenient sign of cough and is a lot easier to diagnose compared to the extra-pulmonary types of TB. Extra-pulmonary TB requires experience to suspect and pin point the location of the disease from patients' signs and symptoms. Without a proper knowledge and experience, medical personnel can easily be diverted to suspect other diseases. For example, pain in the right ankle is more likely to be considered a sprained ankle rather than TB of the joint.

Therefore, the problem with inadequate number of human TB experts that are well experienced in the diagnosis of TB is a major problem in almost all developing countries and needs to be solved.

1.2.2 TB treatment

Tuberculosis treatment is being given in governmental hospitals by a health post funded both domestically and internationally. The following drugs are used as first line treatment of TB [8]:

- Rifampicin(R)
- Ethambutol (E)
- Isoniazid (H)
- Pyrazinamide (Z)
- Streptomycin (S)

Well trained caregivers in the health post follow up the patients through the treatment process. TB treatment medication takes at least six to nine months. The longevity of the treatment makes it very difficult for patients to follow it properly. If TB patients do not get proper follow-up while taking their medication, they could develop resistance to some of the medications and develop multi drug resistant TB (MDR-TB) which is very dangerous.

To overall look into a patient's treatment history and improvement status, record of the patient's state and improvement level should be well documented throughout the treatment. In almost all health facilities, this documentation is kept on paper which is very likely to be torn, faded, destroyed or lost.

Correct and timely diagnosis is very important for a TB patient to start his/her medication as soon as possible in order to fight off the disease before it does permanent damage or lead to death. If TB is not diagnosed early, patients will become weaker and weaker because TB has the tendency to lower their immunity as well as their weight and weakens them to a point that they have to be hospitalized to get their strength back in order to take the TB medications. Therefore, well- educated medical professionals with experience are required to correctly diagnose and treat TB.

1.3 Artificial intelligence

Making intelligent agents take better action by understanding the knowledge around them is the work of Artificial Intelligence (AI). Application areas of AI extends from the simple credit card fraud detection to speech recognition and to the extent of offering advice by recognizing a problem [26]. Major branches of AI are shown in figure 3.

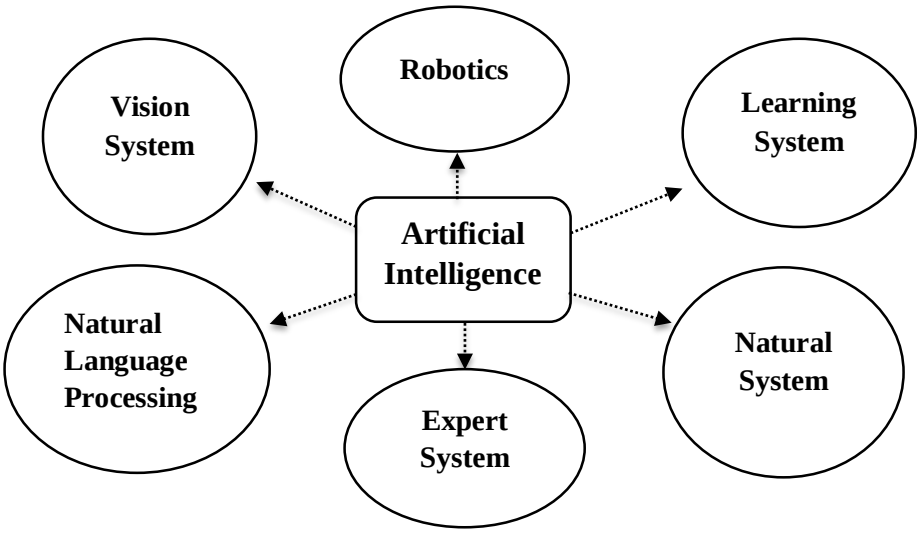


Figure 3: Major branches of AI [27].

1.4 Expert system

This is an intelligent computer program which solves problems that are hard enough to need an expert's involvement to be solved. The general purpose of expert systems is to aid the novice user, less knowledgeable in his domain, to complete his tasks at the level of an expert [28]. Different types of expert systems are shown in figure 4.

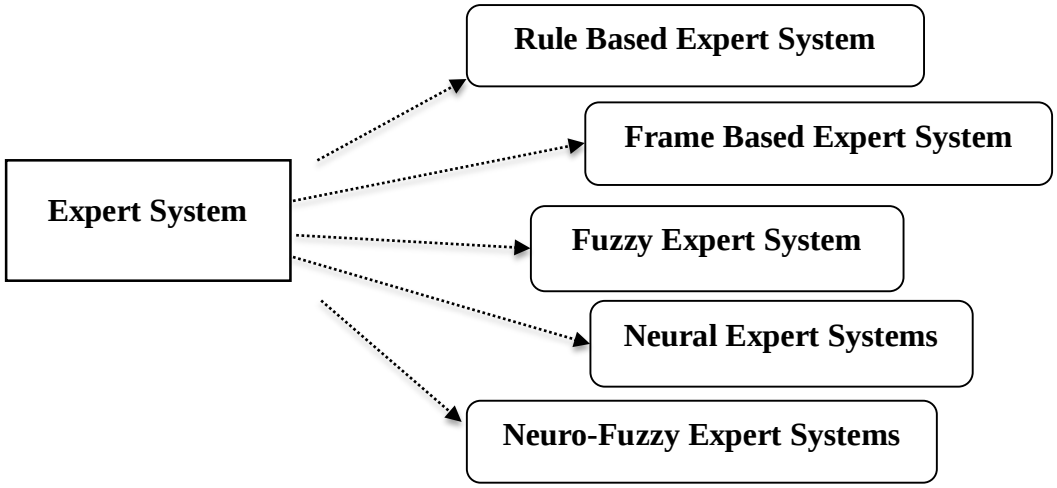


Figure 4: Different types of expert systems [29].

The five types of expert systems are being used in the medical world to assist medical professionals in the diagnosis of different diseases. These expert systems have shown a great deal of advancement in the health sector by increasing accuracy and remarkably decreasing the time and work load of medical personnel.

Among different types of expert systems, rule based and fuzzy expert systems are used as hybrid to design the tuberculosis diagnosis system in the current study.

1.4.1 Rule based expert system

Rule based expert system tries to capture the reasoning capacity of humans. By incorporating expertise, expert systems provide solutions in decisional problems using previous personal experiences [30]. The general architecture of a rule based expert system is shown in figure 5.

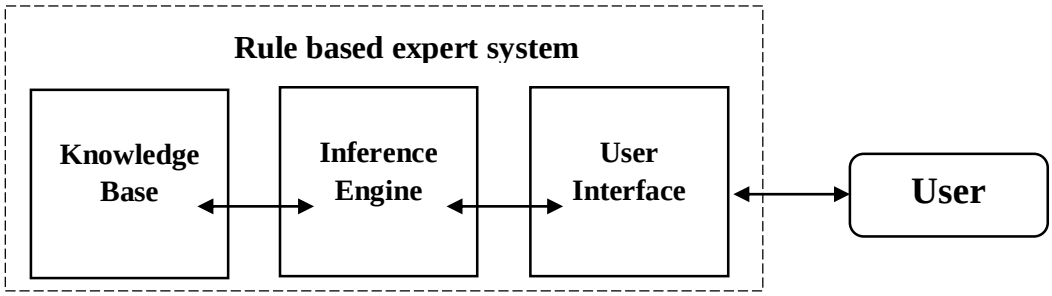


Figure 5: General Architecture of Rule Based Expert System [29].

I. Knowledge base

The quality, completeness, and accuracy of the knowledge obtained determines the outcome of an expert system. The knowledge base acquires this knowledge from an expert and stores it for understanding, formulating and solving problems. “To represent the knowledge, rules, frames, logic, semantic net etc… are used’’ [31].

II. Inference engine

This is the main component of an expert system. It interprets and analyses the antecedent part of each rule in the knowledge base to acquire the firing strength of the rule to arrive at a solution [31].

The inference engine uses these two strategies to forward a solution:

1. Forward chaining

This method uses the strategy of deducing the final solution after considering all the rules and facts [29]. An example of inference mechanism using forward chaining is shown in figure 6.

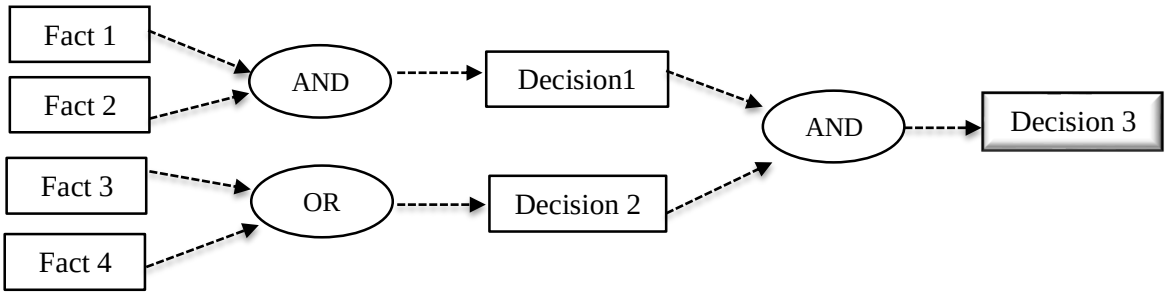


Figure 6: Forward Chaining [32].

2. Backward chaining

This strategy initially considers the conclusion. From the conclusion, it tries to find out which conditions might have led to this result. This strategy finds out cause or reason [29]. An example of inference mechanism using backward chaining is shown in figure 7.

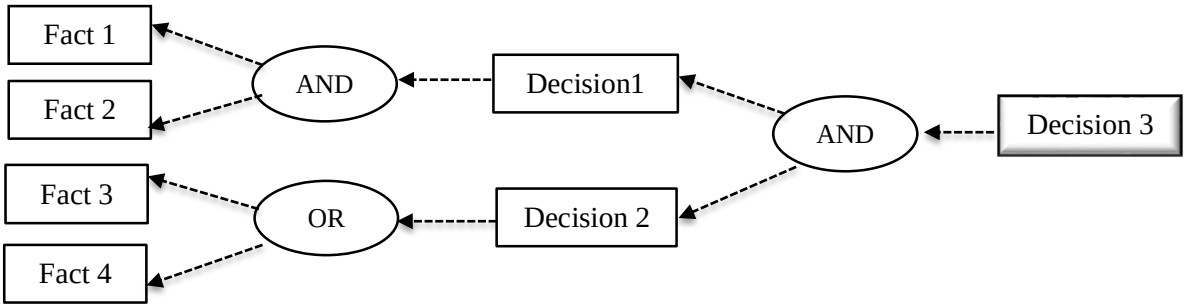


Figure 7: Backward Chaining [32].

1.4.2 Fuzzy expert systems

Fuzzy logic

The term fuzzy as defined in the dictionary means vague, imprecise, not clear or unfocused. In real life, we may come across a situation where we can't decide whether a statement is true or false. For example, when trying to express today's weather, we could say it is cold or hot or chilly. But what does hot, cold or chilly really mean? Expressing the weather like such is imprecise and not clear. The question, how hot or cold the weather really arises.

The medical world is one of the biggest areas dealing with imprecise and vague situations each day. Among the specific areas where imprecise and vague situations take place is in the doctor's office, when the doctor tries to analyze the patients complaints about his/her symptoms.

Fuzzy logic algorithm, just like human decision making, takes into consideration all the data provided and observes all possible values between True and False to give the best conclusion [33].

Fuzzy set

Fuzzy set is a set with no crisp and clearly defined boundaries. Unlike crisp sets with range of function restricted to the values 0 and 1, fuzzy set can contain elements with degree of membership in between completely belonging to the set, which is equal to 1, and completely not belonging to the set, which equals to 0 [33].

A fuzzy set is completely characterized by its membership function (μ) defined as follows [34]:

If X is the Universe of discourse and its elements are denoted as x in contrast with crisp set, then the fuzzy set A of X has characteristics function associated to it.

$\mu_A: X \rightarrow [0,1]$

$\mu_A(x) = 1$ if x is totaly in A

$\mu_A(x) = 0$ if x is not in A

$0 < \mu_A(x) < 1$ if x is partialy in A

Where: X = Universe of discourse

x = elements in X

μ_A = Membership function of fuzzy set A

$\mu_A(x)$ = The degree of belonging to some element x of the universe of discourse X

Membership function

A membership function is a "curve that defines how each point in the input space is mapped to a membership value between 0 and 1." The input space is sometimes referred to as the universe of discourse. These membership values in each fuzzy rule were then taken as weighing factors to find their effect on the conclusion [35].

Membership function of a fuzzy set is usually denoted us $\mu_A$where A is a notation given to the fuzzy set. There are six common types of membership functions: triangular, trapezoidal, gaussian, generalized bell, π- shaped and S- shaped membership function [35].

They differ from one another with respect to shape. The simplest membership functions like triangular and trapezoidal functions are created from straight lines. These two methods have been most commonly used due to their "simple formulas and computational efficiency" [35].

From the two membership functions, triangular membership function is applied in the current thesis work. The reason behind choosing triangular membership function will be explained in the material and method section of the thesis.

Triangular membership function is expressed as follows:

$$\mu_A(x) = \begin{cases} 0 & if \quad x < a \\ \frac{x-a}{m-a} & if \quad a \leq x \leq m \\ \frac{c-x}{c-m} & if \quad m < x \leq c \\ 0 & if \quad x > c \end{cases}$$

Where: a, m, c – are fuzzy triangular parameters

A – is Linguistic Variable

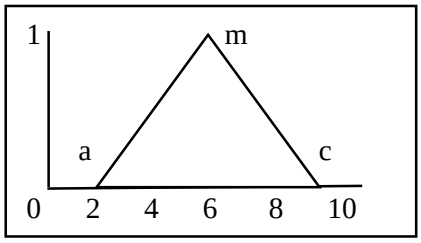


Figure 8: Triangular membership representation [33].

Triangular membership function representation and its shape are shown in figure 8. The horizontal axis represents an input variable x, and the vertical axis defines the corresponding membership value μ(x) of the input variable x [33].

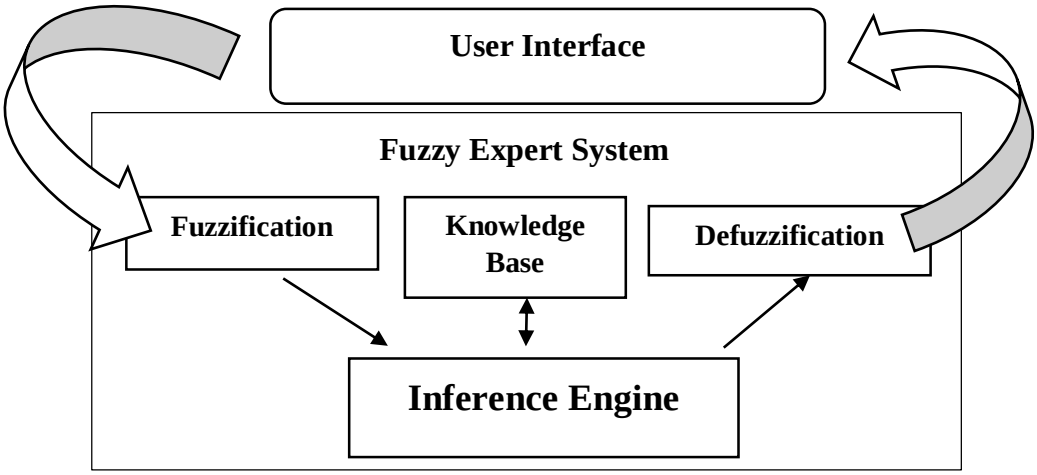


Figure 9: General architecture of fuzzy expert system [36].

I. Knowledge base

The knowledge of an expert is stored in the knowledge base as a form of rules and this knowledge greatly determines how good the system performs [37].

Fuzzy rules

Rules in a fuzzy system reflect the knowledge of experts in a certain field. They are formulated as a "conditional statement" [37]. IF-THEN statements are used to formulate these fuzzy rules to calculate how much the input data matches with the condition in a rule [37].

For example, in the conditional statement:

"IF x is A THEN y is B"

The IF and THEN parts are called antecedent and consequent respectively. X and y are input and output variables respectively while A and B are linguistic variables [37].

II. Fuzzification

"Most variables existing in the real world are crisp or classical variables" [37]. The first step in a fuzzy expert system is the conversion of these variables into fuzzy value. This process is called fuzzification [37].

There are two steps in the fuzzification process. First, membership functions are obtained for the input and output variables. The second step is representing these variables using linguistic variables [37].

Linguistic variables

A linguistic variable is a fuzzy variable whose values are words.

For example: If we say – IF cough is mild THEN TB is moderate;

Mild and moderate, which are the values for the symptom cough and the disease TB, are linguistic variables. These are variables which represent input and output fuzzy variables. They have the concept of fuzzy set qualifiers called hedges. "Hedges are terms that modify the shape of fuzzy sets. They include adverbs such as very, somewhat, quite, more or less and slightly" [29].

III. Fuzzy inference

Fuzzy inference is the process of mapping the given input variables to an output space via fuzzy logic based deducing mechanism. It comprises of "If-Then rules, membership functions and fuzzy logical operations." The usage of IF-THEN rules to reach at a precise value makes fuzzy inference process to resemble human reasoning. Due to this reason, it is widely adopted [33]. There are three types of fuzzy inference methods: mamdani, sugeno and tsukamoto fuzzy inference. These three methods of inference mainly differ in the final process of defuzzyfing the fuzzy output [33]. Mamdani method of inference is widely adopted [33].

IV. Defuzzification

As mentioned in the previous steps of fuzzy inference process, the crisp input from the user goes through fuzzification and gets converted to a fuzzy set to undergo the process of inference to find the fuzzy set aggregated output. Once this is accomplished, the fuzzy set aggregated output must be once again converted into crisp value to be understood by the user. This conversion of fuzzy output to a crisp output is called defuzzification [38].

There are different methods of defuzzification. These methods include: max-membership principle, centroid method, weighted average method, mean max membership method, center of sums and center of largest area and first or last of maxima [39] - [41]. These methods all give a defuzzified final output by applying different techniques to the fuzzy output.

1.5 Image classification

Pulmonary TB as indicated earlier is the major form of TB. It accounts for the large portion of TB cases. Among different examinations which are used to diagnose PTB, Chest X-ray is one. Nowadays, traditional X-ray, which uses film to capture images, is being replaced by a digital one. The digital X-ray is much more efficient, cost effective, and an even safer method for producing diagnostic images [42].

The emergence of the digital radiography paves the way for the development of a computer added image classification method to assist the diagnosis procedure of diseases. Image data sets were prepared by different health organizations using digital images of different body internal structures which are meant to be used for a lot of purposes including diagnostic image classifications.

Machine learning

Machine learning enables computers to execute very complex processes by learning from provided data and experience rather than using "pre-programmed rules" [43], [44]. There are three important types of machine learning algorithms: supervised, unsupervised and reinforcement learning. Different applications of these three learning categories are shown in figure 10.

I. Supervised learning

Supervised learning is the most important type of machine learning. This type of learning is commonly used for labelled datasets. It learns by identifying different features from the input data to give prediction [45].

II. Unsupervised learning

In this type of learning, the datasets are not pre-labelled. Therefore, learning takes place by finding implicit patterns from the data based on the density, structure and other similar segments and features [45].

III. Reinforcement learning

In this type of learning, there is no dataset to train the model with. Instead, it learns from experience to achieve a certain goal which will provide a reward [45].

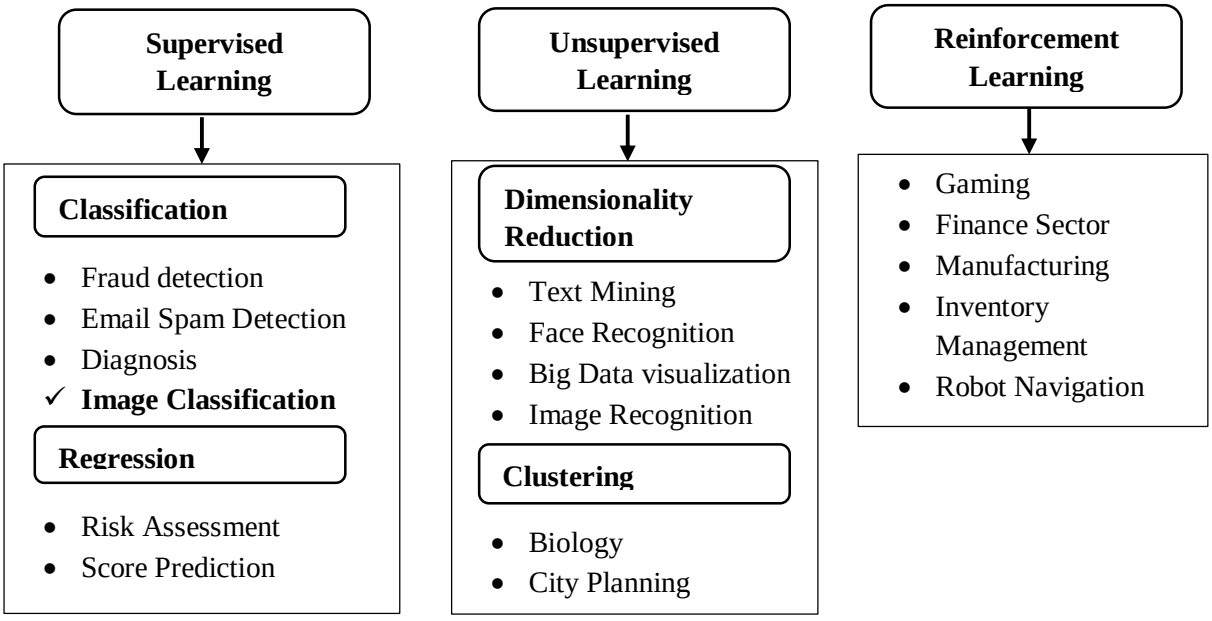


Figure 10: Different application of the three common learning category of machine learning [45].

1.5.1 Deep learning

Deep learning (DL) trains computers to learn how to execute tasks like humans by learning from patterns and basic parameters of a data themselves by using many layers of processing rather than through "predefined equations" [46].

"Deep learning is inspired by the human brain and it consists of artificial neural networks that are modelled on a similar architecture present in the human brain." As its name indicates, learning takes place through deep and hidden multi-layers of interconnected neurons [44].

Artificial neural networks (ANN) are composed of interconnected neurons which work collectively to provide an output by learning from the input [47]. Convolutional Neural Network (CNN) is a special class of ANN which has ground breaking outcome in pattern recognition. This multi-layered neural network recognizes patterns in an image from pixel points following minimum pre-processing steps [46].

There are different CNN Architectures: LeNet, AlexNet, VGG, GoogLeNet, ResNet and more. These architectures are unique in their designs and are being used in "image processing and object recognition" [48]. Among the mentioned CNN architectures, ResNet was chosen to be used in this thesis for image classification of the chest X-ray.

ResNet or Residual Networks is one of CNN's architectures which got a lot more attention and use since 2015 [49]. Different convolutional layers in ResNet 50 are shown in figure 12. ResNet solves many problems related to training deep neural networks.

There are problems while training deeper networks. The deeper the network, the more saturated the accuracy becomes. This is due to the inability to back-propagate the gradients. When the gradients go through continuous multiplication as they are back-propagated, they become infinitely small and vanish. This situation is called the vanishing gradient problem which will cause degradation in performance [49].

ResNet showed that deeper networks can be trained well. It tries to solve the problem of vanishing gradients by applying skip-connections which are shortcut passages for the variants to travel to the earlier layers directly and by implementing heavy batch-normalization. These two techniques enable ResNet to keep its performance while training over thousands of layers [46]. Skip-connections of ResNet is shown in figure 11.

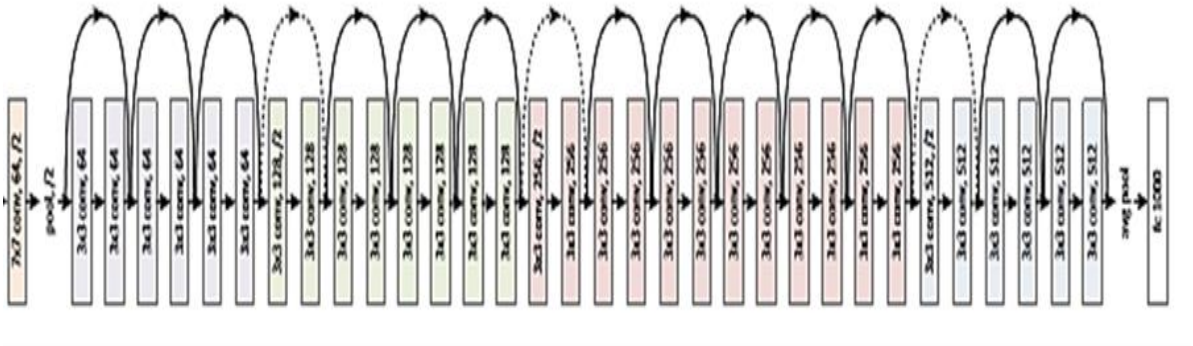


Figure 11: Skip connections of ResNet [48].

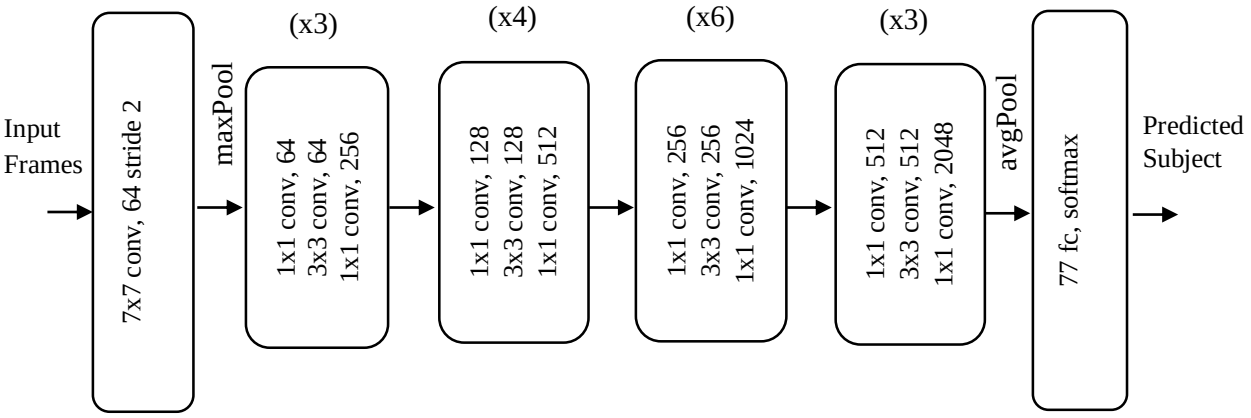


Figure 12: Different convolutional layers in ResNet 50 [50].

In a previous study, "ResNet achieved a top-5 error rate of 3.57%**,** which actually beats human level performance on the dataset" [50]. Despite its deep network, it delivered better performance than most VGGNet architectures. "It bagged all the awards of the ImageNet Large Scale Visual Recognition Challenge (ILSVRC) 2015 over the fields of classification, detection and localization" [50]**.** The above mentioned points about ResNet were the reason behind choosing the network in this thesis for classifying the chest X-ray.

1.6 Statement of the problem

TB is a bacterial infectious disease which is transmitted by droplets containing the bacterium through coughing and sneezing. The primary sites of infection are the lungs, but TB can affect any part of the body.

TB affects adults in their most productive years (15 - 55). This will create individual and socioeconomic burden. Poverty, malnutrition, over-crowded living conditions and high prevalence of HIV infection, which characterize low and middle income countries, have been known for decades to increase the risk of developing the disease. Therefore, even though TB is a global burden, developing countries like Ethiopia are highly affected by the communicable disease, losing millions of lives each year.

Early and accurate diagnosis of tuberculosis is the key to decrease risk of mortality and transmission of the infection. The disease's complicated nature of mimicking others, patient's awareness and perception of the disease, access to health care services, and most importantly inadequate number of experienced health care providers in the field (only around 300 internists in Ethiopia) are among factors that influence the accuracy and time spent in tuberculosis diagnosis. The problem has existed for many decades. But in addition to the above listed problems, due to slow advancement of health sectors with technology of medical diagnostic assistive systems, it has not been solved yet.

Expert systems have been proposed in literatures to minimize errors, work load on medical practitioners and delay in the diagnosis of TB. However, most of the proposed systems have limitations. Some of these limitations include: usage of patient symptoms as the only input which reduces system accuracy since symptom reliability is very low, usage of radiography examination as first stand test which may cause false radiation exposure to patients if conducted with wrong suspicion, not considering different TB variants in their diagnosis and feasibility issue to developing countries since all of the systems were made only considering developed countries where medical practitioners are highly available which contradict our country's situation.

Generally speaking, there is no system for full diagnosis of TB which incorporates accuracy, reduces diagnostic delay and misdiagnosis cases, and contains a patient data recording system for follow-up by taking into consideration the inadequate number of medical professionals and low economic status of developing countries. The research, by taking into consideration the above mentioned problems, will try to forward a design solution to achieve WHO's Goal of ending TB epidemic by 2030 which Ethiopia is following.

1.7 Objectives

1.7.1 General objective

The general objective of this research is to design a hybrid fuzzy and rule based expert system for accurate diagnosis of tuberculosis.

1.7.2 Specific objectives

The specific objectives of this research are:

- To characterize the distinct features of PTB from other TB mimicking diseases
- To design a hybrid of fuzzy and rule based expert system for accurate diagnosis of TB
- To evaluate the capability of fuzzy expert system in dealing with ambiguous inputs
- To evaluate the potential of hybrid systems for the diagnosis of TB
- To design a data recording system for improved patient follow up and easy access to data
- To evaluate the performance of designed expert system in minimizing diagnostic delay, misdiagnosis cases and filling the gap created by inadequate number of experienced medical personnel

1.8 Scope of the study

The research starts by gathering relevant data using both primary and secondary sources. The data will be gathered on problems in the diagnostic as well as treatment procedure, different situations leading to misdiagnosis, input data for the system and selection of the appropriate tests to diagnose TB using both qualitative and quantitative research methodologies.
Identification of symptoms of different types and classes of TB will be done by direct contact with human TB experts. Besides referring manuals prepared in the federal level, comparison among knowledge of different human experts on the field will be made to increase data accuracy. Selection of the best tests to accurately diagnose TB and its complications will be done with the help of laboratory physicians and TB experts. After refining the data and identifying the accurate and useful ones, the research will extend its scope to designing the TB diagnosis assistive system. The final step of the designing process, which is system accuracy verification, will be done quantitatively using real time TB cases. Finally, it is believed that the expert system will be applied and be of great use to all governmental hospitals and health centers with computer access.

CHAPTER TWO

Literature review

The involvement of Artificial Intelligence (AI) in the diagnostic world goes a few decades back. Since then, it has made a tremendous advancement in assisting health professionals in the accurate diagnosis of different diseases. In this section, different works done with the purpose of assisting the diagnosis of TB will be reviewed and the gaps in these studies, which are initiatives to this research, will also be stated.

2.1 Review of expert systems designed for the diagnosis of tuberculosis

Neural networks (NN) were used to design expert systems with the purpose of assisting the diagnosis of tuberculosis in previous studies [51], [52]. "Back-propagation with momentum and Levenberg-Marquardt (LM) algorithms were used to perform the task of training in the multi layered neural network (MLNN)" [51]. In this work, thirty eight input features were used which include symptoms and different laboratory tests. In another study, "general regression neural network (GRNN) was used in the development of predictive model" [52]. This model is comprised of an input, a hidden and an output layer. The input patterns are formed by 21 distinct parameters; demographic variables, constitutional symptoms, and radiographic findings [52].

In these two approaches, their usage of NNs has a high tendency of leading to overfitting when trying to increase the number of hidden neurons in order to improve the "processing power of the network." When the model overfits, it will learn the noise in the data in addition to the training set, leading to poor generalization. Since the model is designed for a population with a specific type of TB epidemiology, its application for different scenarios is questionable. In addition, the model does not include different classification of TB; instead, it was only designed for PTB diagnosis. On the other hand, the two NN models do not consider the ambiguity created while using signs and symptoms as an input.

Aside from the methodology used, the different examinations used in the mentioned works, especially the first one [51], used over 25 different laboratory tests to only diagnose PTB with the aim of just increasing system accuracy which is irrelevant and causes wastage of time and resources as well as money.

Fuzzy logic is another branch in which the medical world is benefiting from. Different fuzzy expert systems have been developed to assist medical personnel in the diagnosis of tuberculosis [53] - [55]. A rule–based fuzzy diagnostics decision support system was used to assign class labels for tuberculosis [53]. The decision support system contains 323 sets of rules for the determination of the class of tuberculosis. This system was believed to aid the diagnosis of the different classes of tuberculosis [53]. However, usage of symptoms to arrive at a diagnostic conclusion and the prescription of medication without including different diagnostic examinations might lead to the misdiagnosis of cases, which is what the work was trying to avoid in the first place.

Fuzzy cluster means expert system was designed for the diagnosis of TB [54]. It has different clusters to categorize the seven forms of TB. Elements in those different classifications of TB were categorized in the clusters based on their similarity. The expert system consists of a knowledge base which holds the symptoms for TB and a fuzzy c-means inference engine. The system does not include pulmonary TB which accounts for 65 – 85 % of TB cases [8]. Different forms of TB share symptoms which can be seen in most cases. Therefore, categorizing the different classification of TB in clusters is not that much significant at this point.

The other work done in this area was a TB diagnosis and treatment system [55]. The system has 18 input and 5 output fields. Input fields are chosen symptoms for the 5 groups of TB and each of the five output variables have three fuzzy sets, which represent the low, medium and high level of TB. The system uses triangular membership function, mamdani inference and center of gravity method of defuzzification. The designed system has been tested with an expert-doctor. However, the four chosen extra-pulmonary TB diseases have their own symptoms which characterize each one of them. Using one or two symptoms which are specific to the four diseases has a high chance of causing misdiagnosis even if fuzzy logic is applied to deal with the imprecise situations. The system only uses symptoms to reach at a diagnostic conclusion, which will decrease the accuracy of the overall diagnosis.

Rule based expert systems (RBES) are also being used to assist medical professionals in their hard work of disease diagnosis. RBES was used to assist the diagnosis of tuberculosis in previous studies [56] - [58]. A RBES was developed for the “diagnosis of five diseases, namely: malaria, typhoid fever, cholera, tuberculosis, and breast cancer” [56]. The proposed expert system used forty three signs and symptoms as input and contained 46 rules.

The system has a knowledge base in which the rules are saved in, and an inference mechanism to process the input to indicate which one of the five diseases is being experienced by the patient [56]. The five diseases which are diagnosed by the system greatly differ from one another. This will prevent the system from achieving better performance and accurate diagnosis of each of the diseases.

On the other hand, a belief rule based expert system (BRBES) to assess tuberculosis under uncertainty was also designed [57]. The system contains a knowledge base which uses belief rule base to "represent the domain knowledge under uncertainty" and an inference engine which transforms the input, calculates the weights and activates the rule which has firing strength and finally aggregates the output of each rule by using evidence based reasoning. [57]. The major gap in the above mentioned two works is using rule based expert system to deal with imprecise and vague inputs, like symptoms. Unlike fuzzy logic, rule based expert systems have a hard time generalizing based on indefinite data. Therefore, usage of such systems on patients' symptoms to reach at a diagnostic conclusion will create questionable system accuracy.

The other rule based expert system is a mobile application for the diagnosis and treatment of TB [58]. The proposed tool was developed based on a step by step conditional approach which helps the user to find out whether he/she has TB. The output was based on the symptoms and a tuberculin skin test which is performed by the user himself [58]. The mobile application has questionable system accuracy because the system tries to use RBES to deal with imprecise patient inputs. In addition to the gap mentioned above, the application requires some level of the user's (non-clinician) knowledge. This all makes it difficult to apply for developing countries like Ethiopia, where the technological, economic and educational level of the larger society is very low.

2.2 Review of literatures on chest X-ray image classification for the diagnosis of PTB

Convolutional neural networks are being used for image classification in the diagnosis of different abnormalities. Different works for the detection, localization and classification of different abnormalities on chest x-rays have been done [59] - [62]. Deep convolutional neural network for the detection and localization of abnormalities in chest X-rays was designed using two publicly available datasets [59].

Deep convolutional neural networks (DCNN) in the diagnosis of different abnormalities were analysed to have different levels of performance. This work shows that it is possible to achieve consistent detection for small number of training examples by performing many train-tests with random data split by using average values as accuracy measures. It has been shown that shallow features or earlier layers consistently provide higher detection accuracy compared to deep features. Accuracy, sensitivity and specificity of different models including Rule Based Features, Alex Net, Vgg-16, Vgg-19, Resnet-50, Resnet-101 and Resnet-152 for Tuberculosis detection using Shenzhen Dataset was clearly stated. A promising level of accuracy was achieved [59].

Another chest X-ray classification using Convolutional Neural Network (CNN) models to detect pulmonary tuberculosis (PTB) manifestation was designed [60]. Identification of TB manifestation on Montgomery County (MC) and Shenzhen (SH) chest X-ray datasets was done by using the four CNN models which are VGG-16, VGG-19, ResNet50 and GoogLenet. This work assesses the limit of accuracy with the four CNN models and gives a clear image of the accuracy level which can be achieved using the stated two datasets [60].

A deep learning X-ray image classification system was also designed for potential tuberculosis patients [61]. Different types of learning rate enhancement techniques were used. Different models were fine-tuned using multiple data augmentation techniques. The model was trained on a large, low resolution national institute of health (NIH) dataset first and was fine-tuned on a small, high resolution china-Montgomery datasets. Then, the model classified each image into fourteen different lung diseases [61].

On the other hand, automated detection of multiple lesions on chest X-ray images was designed in the present year of 2020 [62]. In this paper, neural network technique with association-specific contexts was used to classify the different lesions on a chest X-ray. To detect different chest lesions using both image and text information, CNN and short-term memory network were used by an attention mechanism called “CNN-ATTENTION-LSTM (CAL) network.” CAL network acquired a better prediction: 85.4% precision, recall and F-score value in the case of atelectasis and infiltration because of its ability to give possible clinical relationship between lesions [62].

The above stated four works have shown very good potentials in the diagnosis of pulmonary tuberculosis by using chest X-ray.

Different data sets were compared and contrasted and based on the accuracy level achieved with the mentioned data sets, the best ones were suggested in the works. Among those data sets Montgomery County and Shenzhen data sets were chosen to be applied in this research. Unlike the four literatures mentioned above, by focusing on the diagnosis of pulmonary tuberculosis and by using ResNet 50 pre-trained convolutional neural network, which gives a remarkable accuracy as mentioned in the literatures [59], [61], a chest X-ray classification model is designed as one of the examination modalities for the diagnosis of tuberculosis in this research .

Generally, by filling the gaps in the literatures, by taking positive motivational methodologies and considering problems witnessed during the research in the current diagnosis procedure of TB, an assistive decision support expert system with a chest x-ray image classification feature for the diagnosis of TB was developed which could be applied in most of the hospital settings of countries like Ethiopia.

Table 1: General view to the works of the literatures reviewed.

No	Paper	Design purpose	Methodology used	Gap of the works
1	**TB disease diagnosis using artificial neural network [51]**	For analysis of tuberculosis	Artificial neural network	• Poor generalization (Overfitting) • Absence of explicit relationship between input and output data • Have not considered the uncertainty issues associated with signs and symptoms • Model does not consider extra-pulmonary tuberculosis which has the highest tendency of getting misdiagnosed by doctors
2	**Predicting active pulmonary tuberculosis using artificial neural network [52]**	Tuberculosis predictive model	General Regression Neural Network (GRNN)	
3	**Diagnostics decision support system for TB using fuzzy logic [53]**	Algorithm used to find the probable class of tuberculosis	Fuzzy logic	• Does not give full TB diagnosis by considering different types • Does not incorporate examinations(Questionable system accuracy)
4.	**Fuzzy cluster means expert system for the diagnosis of tuberculosis [54]**	For the diagnosis of different forms of TB	Fuzzy cluster means	• Using cluster for different forms of TB is not appropriate since they share symptoms • Does not incorporate examinations (Questionable system accuracy)
5	**Efficient fuzzy-based system for the diagnosis and treatment of tuberculosis [55]**	For the diagnosis of four extra-pulmonary diseases	Fuzzy logic	• Only using one or two symptoms which are specific to a diseases has a high chance of causing misdiagnosis • Does not incorporate examinations (Questionable system accuracy)
6	**Rule-based expert system for disease diagnosis [56]**	Diagnose malaria, typhoid fever, cholera, tuberculosis, and breast cancer	Rule-based expert system	• Using rule based expert system to deal with imprecise and vague inputs, like symptoms (Questionable system accuracy)
7	**A belief rule based expert system to assess TB under uncertainty [57]**	For the diagnosis of tuberculosis	Rule based expert system	• Using rule based expert system to deal with imprecise and vague inputs, like symptoms (Questionable system accuracy)
8	**Expert system for clinical diagnosis of TB** (Android application) **[58]**	Indicate the probability of a person having TB to go to health facility	Rule-based expert system	• Using rule based expert system to deal with imprecise and vague inputs, like symptoms • Not feasible to developing countries

CHAPTER THREE

Material and Methods

In this chapter, the materials and methods used to collect the inputs to the system, the techniques and methods followed to design the diagnostic system are clearly described. It also discusses the study population and sampling technique used to select the individuals on which the system is tested on.

3.1 Study area

The research was conducted in St. Peter's specialized hospital, Alert hospital and Bole sub city health center all found in Addis Ababa, Ethiopia. 60 patients, aged between 15 and 80 were selected from St. Peter's and Alert Hospitals having TB and 20 patients who were normal or having pneumonia, asthma or COPD diseases. Sample of patient data collection form is presented in Appendix (IV). Honest attempt was made to examine the patients' data using the designed system.

3.2 Study period

This research was conducted from May 2018 – September 2020, G.C including the data collection period.

3.3 Study design

To acquire relevant data for designing the system, both primary and secondary sources of data were used and qualitative as well as quantitative research strategies were conducted.

Qualitative research strategy was used to find the right symptoms of different TB classifications and major TB mimicking diseases which are inputs for the system. Primary source of data such as questionnaire, direct observation and interview of the target groups were used to collect the mentioned data. Different websites, journals, books and guidelines for TB diagnosis were also used as secondary sources of data.

The choice of laboratory and radiology examinations for accurate diagnosis of TB was made quantitatively with the help of laboratory technicians and doctors.

3.4 Study population

Pulmonary TB patients, extra-pulmonary TB patients, asthma patients, pneumonia patients and COPD patients and healthy people.

3.5 Sampling procedure

Purposive non-probabilistic sampling technique was used to choose patients diagnosis data for formulating the rules and evaluating the system. Purposive sampling technique is a non-probabilistic sampling in which the researcher chooses the participants as per his/her own judgment, keeping back in mind the purpose of the study [63]. The choice of sample subjects in the research was made purposively with regard to their age and diagnosis history.

3.6 Study variables

3.6.1 Dependent variable

Accuracy of fuzzy and rule based hybrid expert systems for the diagnosis of tuberculosis.

3.6.2 Independent variables

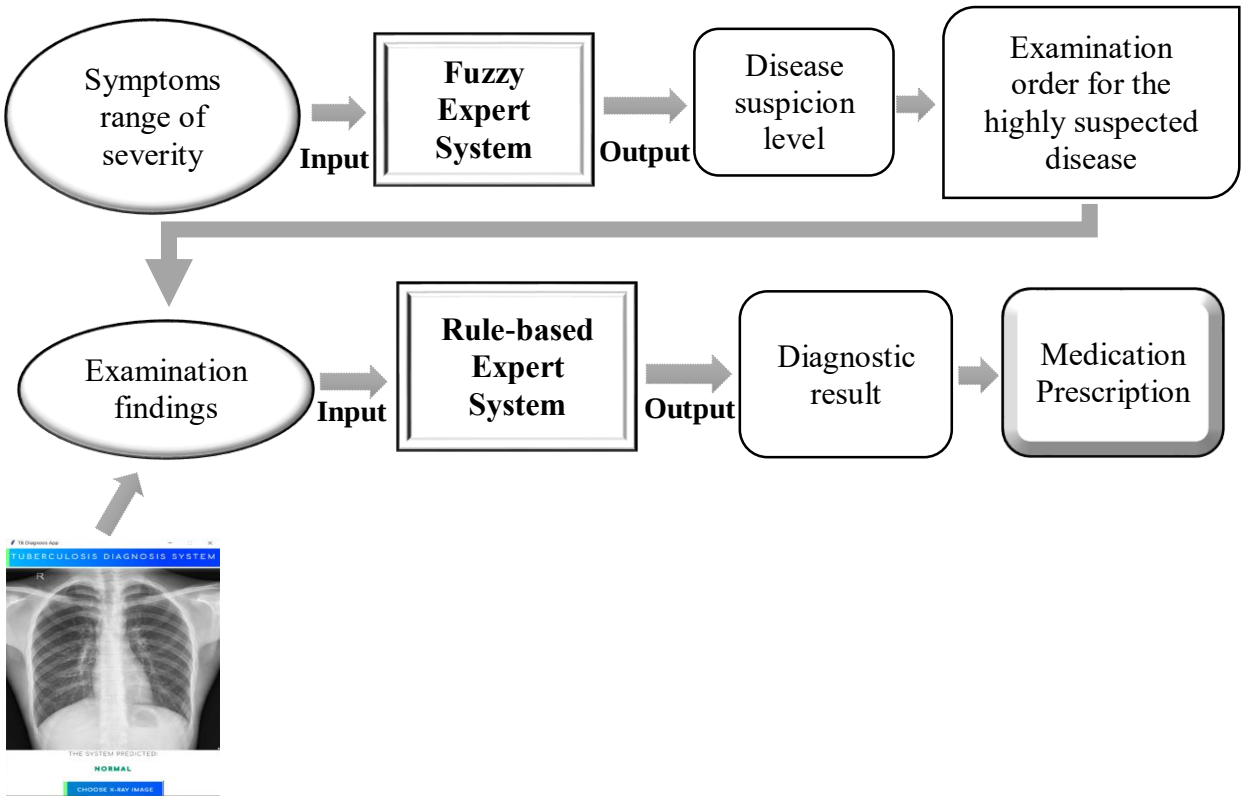
- The choice of symptoms
- Tests used for the diagnosis
- The fuzzy and rule based methods used
- Overall execution time of the system

3.7 The designed expert system

To assist the diagnosis procedure of TB, expert systems which provide solutions in decisional problems after getting the knowledge from human experts were used. Expert systems as mentioned in the background section have many classifications, among which rule based and fuzzy expert systems were used as hybrid to design the tuberculosis diagnosis system. Hybrid expert system is the combination of two or more types of intelligent systems [29]. Python, an interpreter, object-oriented, high-level programming language was used to design the expert system.

The choice of the fuzzy expert system is due to its ability to deal with imprecise and vague situations, which makes it suitable for disease diagnosis using a patient's symptoms. On the other hand, the rule based expert system is used to analyse the examination findings to reach at a final diagnosis result since such expert system works well with non-ambiguous and precise inputs. Moreover, the transparency of TB diagnosis is ensured by these two types of expert systems since they provide clear relationship between input and output data.

The general architecture of the designed expert system and a detailed work flow of the two expert systems (Fuzzy and Rule-based expert systems) used are shown in figure 13.



Chest X-ray image classification

(A)

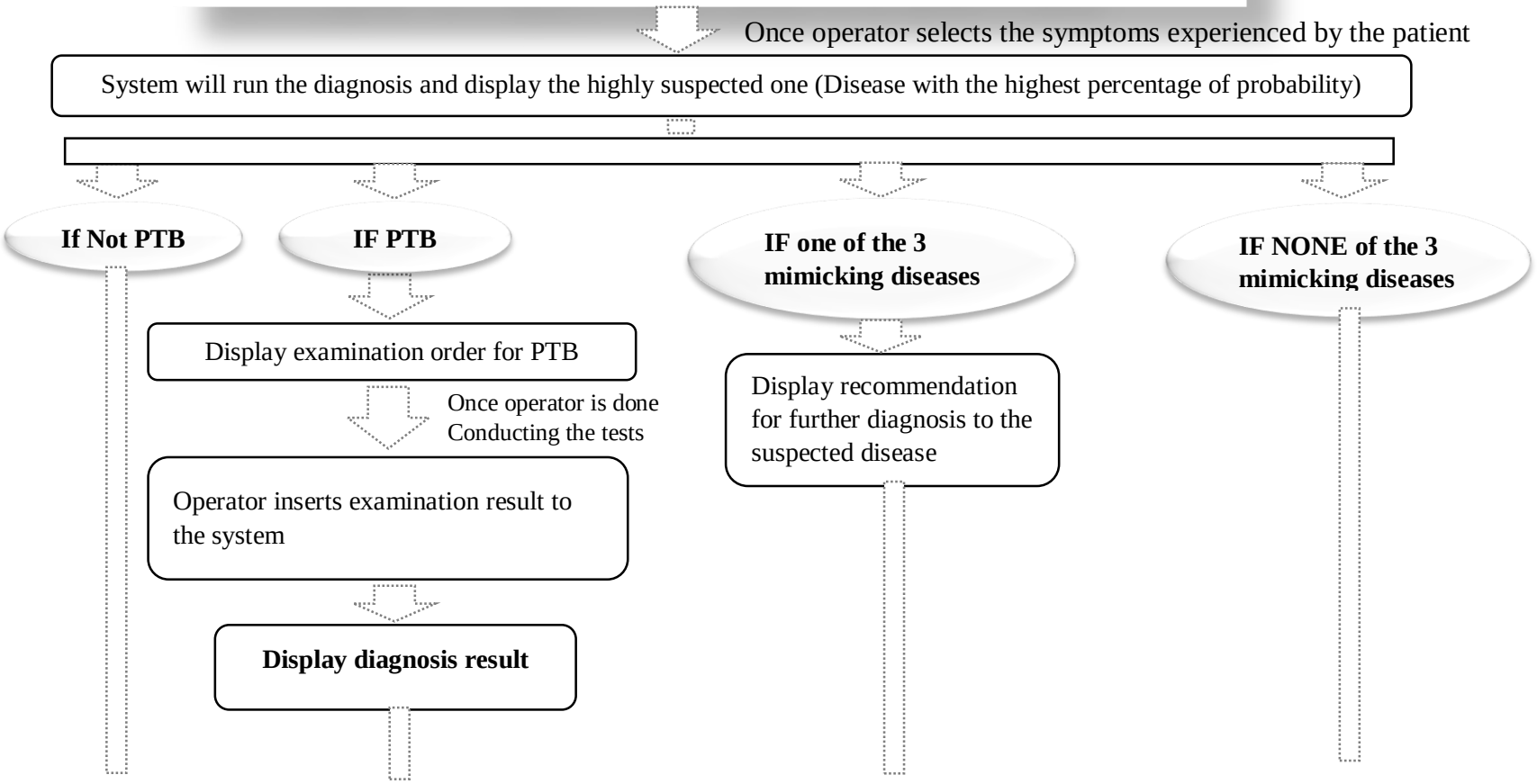
1st Fuzzy System (PTB, COPD, Pneumonia and Asthma)

Input

The mentioned 4 diseases symptoms

- Severity level (Mild, Moderate or Severe) and
- Their respective range of severity (0-10)

(List of symptoms will be displayed in the user interface for the operator to choose)



(B)

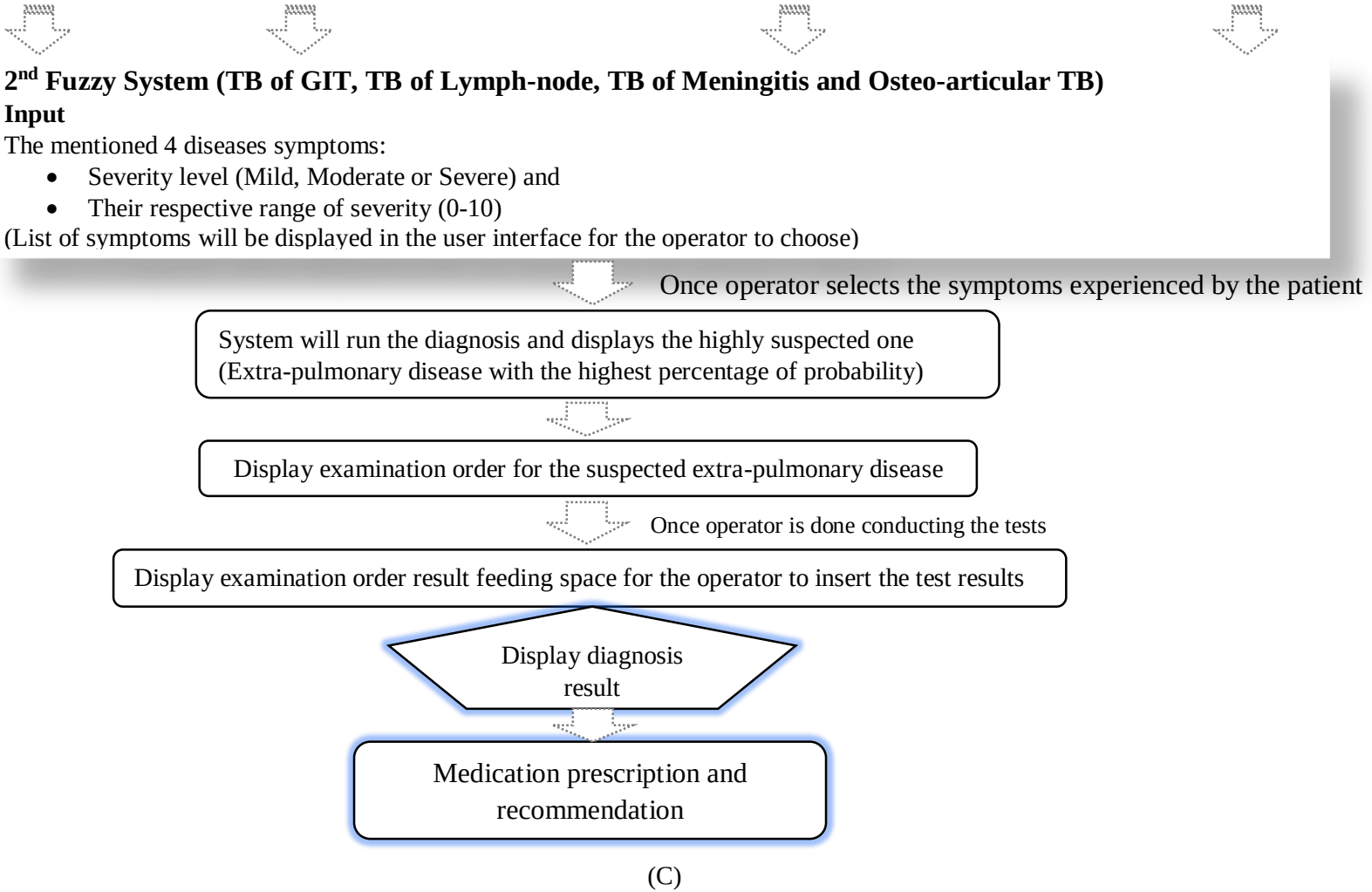


Figure 13: Overall architecture and work flow of the designed system A) General architecture of the designed expert system B) 1st fuzzy system (PTB, COPD, pneumonia and asthma), C) 2nd fuzzy system (TB of GIT, TB of lymph-node, TB of meninges and osteo-articular TB).

3.7.1 The fuzzy expert system design

The medical world is one of the biggest areas dealing with imprecise and vague situations each day. Doctors struggle to get a clear image of the actual level or precise feeling of the patient with words like “I have headache or cough or confusion,” which may lead to wrong conclusion. Such cases and many more are the basis of the need for decision support systems. This is where the fuzzy logic comes in, which offers very valuable flexibility for reasoning. The architecture of the designed fuzzy expert system is shown in figure 14.

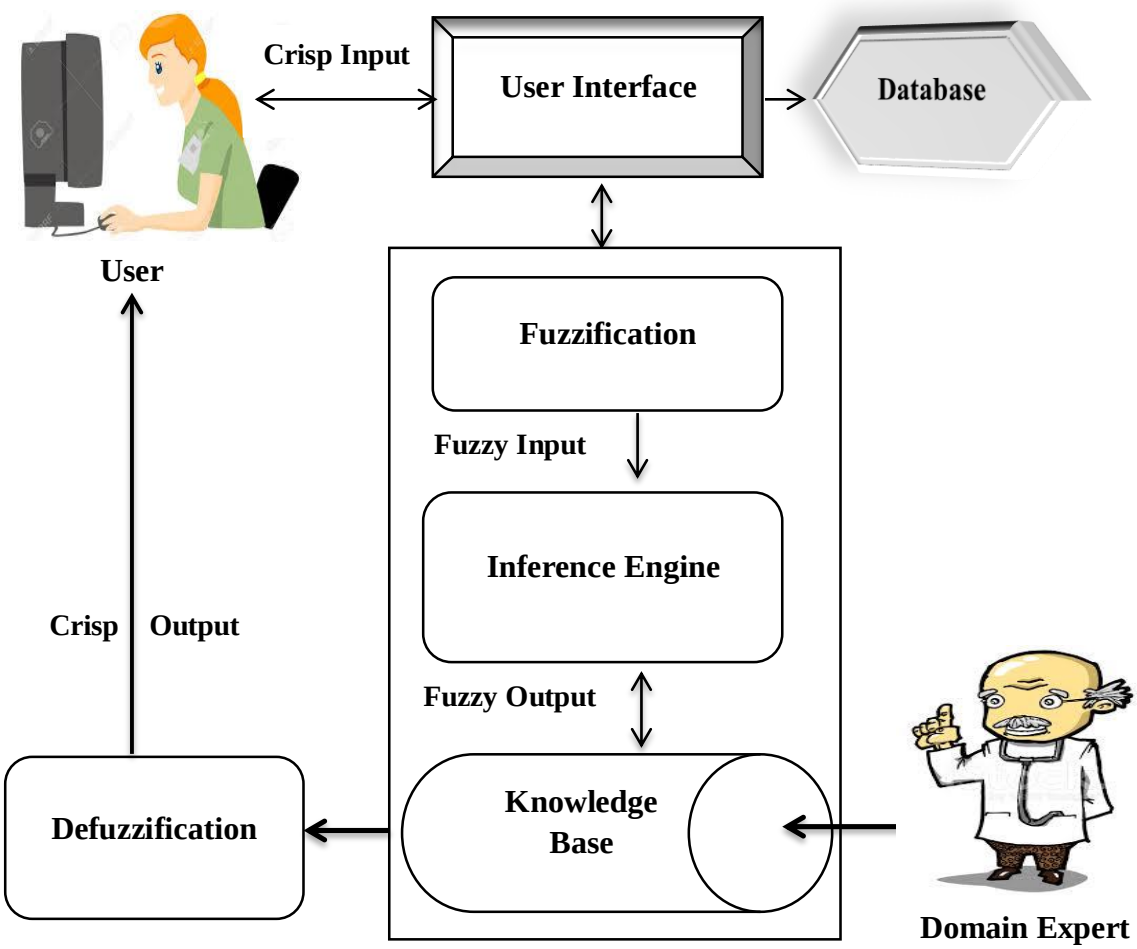


Figure 14: Architecture of the designed fuzzy expert system.

The developed algorithm for the fuzzy diagnostic process of TB has the following steps:

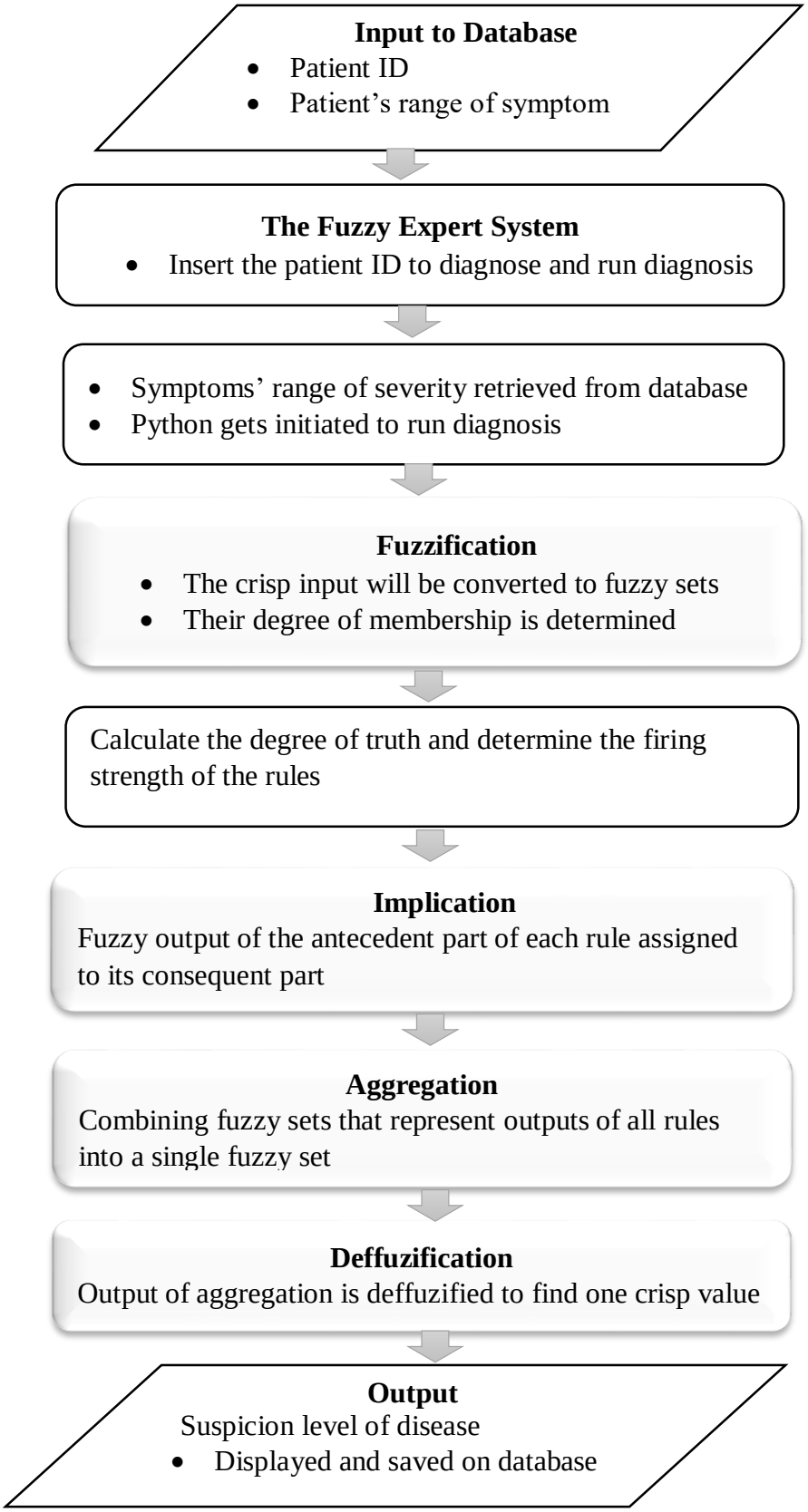


Figure 15: The steps followed in designing the fuzzy portion of the decision support system.

I. Domain expert

A person with knowledge and expertise, especially on the specific area which the system is designed for, is called a domain expert. Three doctors from Alert and St. Peter's specialized hospitals who have years of experience working with TB and cough related diseases were the domain experts in the current thesis work. The knowledge of the experts is used to design the system, mainly the knowledge base which stores the knowledge in the form of rules from which the system will infer and lookup to make decisions.

II. Knowledge base of the fuzzy expert system

With the help of the three experts, input data to the fuzzy expert portion of the system was collected. This input contains symptoms that are highly suggestive of pulmonary TB, the chosen TB mimicking diseases and extra-pulmonary TB as shown in table 2 and 3.

Table 2: The chosen symptoms for the first fuzzy system of cough related diseases.

No	Symptoms for PTB	Symptoms for Asthma	Symptoms for Pneumonia	Symptoms for COPD
1	Cough	Cough at night or with environmental stimuli	Cough	Cough
2	Chest pain or tightness	Shortness of breath especially at night or with environmental stimuli	Confusion	Wheezing
3	Unintentional weight loss	Wheezing	Respiratory rate	Shortness of breath
4	Respiratory rate		BP	Fever
5	Shortness of Breath		Age	Edema

Table 3: The chosen symptoms for the second fuzzy system of the chosen EPTB diseases.

No	Symptoms for TB of GIT	Symptoms for TB of Lymph-node	Symptoms for Osteo-articular TB	Symptoms for TB of Meninges
1	Loss of appetite	Mass along the nick	Restriction of movement	Stiff Neck
2	Abdominal pain	Unintentional Weight loss	Pain or stiffness	Weakness
3	Change in bowel habit	Fever	Swelling of joint	Altered mental status
4	Nausea		Headache &/or fever	Meningeal signs
5	Abdominal swelling		Draining sinus	Headache &/or fever

Once the inputs to the fuzzy expert system have been collected, the next step is using the appropriate fuzzification, inference and deffuzification methods to formulate the fuzzy diagnostic system.

The choice of the methods applied in the research was made based on the input used, the desired output and the functionality of the methods as observed on previously applied works with the aid of expert doctors in the field of TB.

III. Fuzzification

The first step in the development of fuzzy logic based expert system is to construct fuzzy sets for the parameters. On the basis of the domain expert's knowledge, the input and output parameters selected to describe the intensity level of specific symptoms and diseases were three linguistic variables namely: mild, moderate and severe.

The fuzzy variables or symptoms chosen, the linguistic variables with which each symptom's intensity level was expressed, representation of each linguistic variable and their respective ranges are shown in table 4 and 5.

Range of Fuzzy values for PTB, pneumonia, asthma and COPD

Table 4: Range of fuzzy values for PTB, pneumonia, asthma and COPD.

No.	Fuzzy Variables	Linguistic Variables	Linguistic Variables representation	Fuzzy Triangular ranges
1	Cough	Mild	Dry	[0, 0, 5]
		Moderate	With sputum	[1, 5, 9]
		Severe	With sputum & blood	[5, 10, 10]
2	Wheezing	Mild	Only wheeze	[0, 0, 5]
		Moderate	Wheeze with shortness of breath	[1, 5, 9]
		Severe	Wheeze with hypoxia	[5, 10, 10]
3	Shortness of Breath	Mild	At ordinary activity	[0, 0, 5]
		Moderate	At minimal activity	[1, 5, 9]
		Severe	At rest	[5, 10, 10]
4	Fever	Mild	37.5 - 38.5 ºC	[0, 0, 5]
		Moderate	38.5 - 40.5 ºC	[1, 5, 9]
		Severe	>40.5 ºC	[5, 10, 10]
5	Edema	Mild	Grade I	[0, 0, 5]
		Moderate	Grade II	[1, 5, 9]
		Severe	Grade III	[5, 10, 10]
6	Cough at night or with environmental stimuli	Mild	Not frequent	[0, 0, 5]
		Moderate	Frequent at day time	[1, 5, 9]
		Severe	Frequent at day and night time	[5, 10, 10]
7	Shortness of breath especially at night or with environmental stimuli	Mild	Not frequent	[0, 0, 5]
		Moderate	Frequent at day time	[1, 5, 9]
		Severe	Frequent at day and night time	[5, 10, 10]
8	Confusion	Mild	Disoriented to time	[0, 0, 5]
		Moderate	Disoriented to place	[1, 5, 9]
		Severe	Disoriented to person	[5, 10, 10]
9	Respiratory rate	Mild	18-20 breath/min	[17, 17, 26]
		Moderate	20-25 breath/min	[18, 26, 34]
		Severe	>25 breath/min	[26, 35, 35]
10	BP	Mild	70/60 - 90/60 mmHg	[0, 0, 5]
		Moderate	< 70/60 mmHg	[1, 5, 9]
		Severe	Un recordable	[5, 10, 10]
11	Age	Mild	Adult	[0, 0, 5]
		Moderate	Child < 14	[1, 5, 9]
		Severe	Old > 65	[5, 10, 10]

12	Chest pain or tightness	Mild	At ordinary activity	[0, 0, 5]
		Moderate	At minimal activity	[1, 5, 9]
		Severe	At rest	[5, 10, 10]
13	Unintentional weight loss	Mild	< 5% of persons weight	[0, 0, 10]
		Moderate	5-10% persons weight	[1, 10, 19]
		Severe	10 - 20% persons weight or more	[10, 20, 20]

Range of Fuzzy values for TB of GIT, TB of osteo-articular, TB of meninges and TB of lymph-node

Table 5: Range of fuzzy values for TB of GIT, TB of Osteo-Articular, and TB of Meninges and TB of Lymph-node.

No.	**Fuzzy Variables**	**Linguistic Variables**	**Linguistic Variables representation**	**Fuzzy Triangular ranges**
1	Stiff Neck	Mild	< 1 day	[0, 0, 5]
		Moderate	1day – 3days	[1, 5, 9]
		Severe	> 3 days	[5, 10, 10]
2	Meningeal signs	Mild	Only one Sign	[0, 0, 5]
		Moderate	Two Signs	[1, 5, 9]
		Severe	Three Signs	[5, 10, 10]
3	Altered mental status	Mild	Disoriented to time	[0, 0, 5]
		Moderate	Disoriented to place	[1, 5, 9]
		Severe	Disoriented to person	[5, 10, 10]
4	Weakness	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
5	Headache &/or fever	Mild	Intermittent headache or/and 37.5-38.5 ºC fever	[0, 0, 5]
		Moderate	Persistent headache or/and 38.5-40.5 ºC fever	[1, 5, 9]
		Severe	Morning headache with vomiting or/and >40.5 ºC fever	[5, 10, 10]
6	Mass along the nick	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
7	Unintentional weight loss	Mild	< 5% persons weight	[0, 0, 10]
		Moderate	5-10% persons weight	[1, 10, 19]
		Severe	10 - 20% persons weight or more	[10, 20, 20]

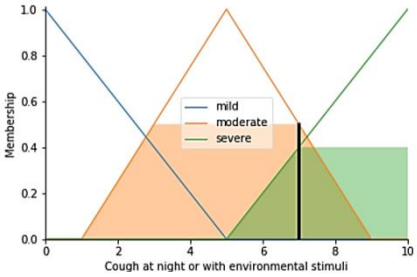
8	Fever	Mild	37.5 - 38.5 ºC	[0, 0, 5]
		Moderate	38.5 - 40.5 ºC	[1, 5, 9]
		Severe	>40.5 ºC	[5, 10, 10]
9	Swelling of joint	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
10	Restriction of movement	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
11	Pain or stiffness	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
12	Draining sinus	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
13	Abdominal pain	Mild	< 2 weeks	[0, 0, 5]
		Moderate	> 2 weeks	[1, 5, 9]
		Severe	> 1 month	[5, 10, 10]
14	Change in bowel habit	Mild	Diarrhea	[0, 0, 5]
		Moderate	Constipation	[1, 5, 9]
		Severe	Both	[5, 10, 10]
15	Loss of appetite	Mild	Occasional	[0, 0, 5]
		Moderate	Most of the time	[1, 5, 9]
		Severe	Always	[5, 10, 10]
16	Abdominal swelling	Mild	<1 month	[0, 0, 5]
		Moderate	1 month – 6 months	[1, 5, 9]
		Severe	>6months	[5, 10, 10]
17	Nausea	Mild	Occasional	[0, 0, 5]
		Moderate	Most of the time	[1, 5, 9]
		Severe	Always	[5, 10, 10]

The fuzzification process starts with transformation of the raw data to fuzzy sets. In the process, linguistic variables were evaluated using triangular membership function. The choice of the triangular membership function was made by comparing the output obtained while using the different types of membership functions as shown in figure 16 and 17.

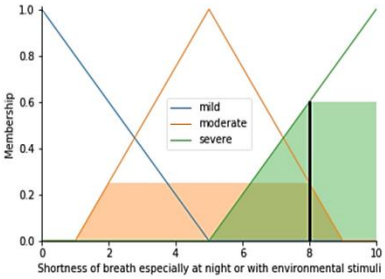
Triangular and gaussian membership functions were applied on different ranges of asthma symptoms. The final output found by applying the two membership functions was then evaluated by the experts.

As an example for the three symptoms of asthma (cough at night or with environmental stimuli, shortness of breath especially at night or with environmental stimuli and wheezing), moderate (7), severe (8) and mild (1) range of symptoms were given respectively.

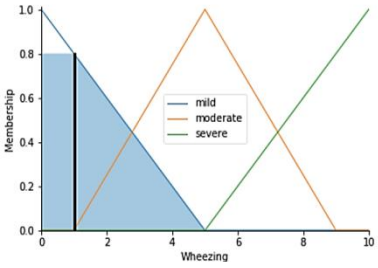
For the inputs stated above, the system has given the severity level of asthma to be 6.463 while applying triangular membership function.



Input 1 = 7

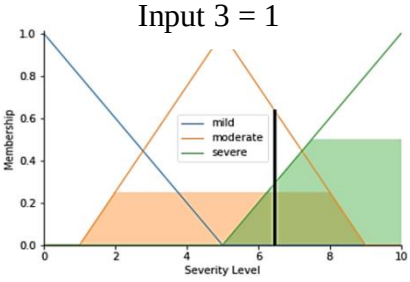


Input 2 = 8



Input 3 = 1

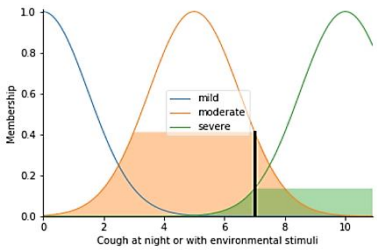
```
Cough_at_night_or_with_environmental_stimuli: 7
Shortness_of_breath_especialy_at_night_or_with_
environmental_stimuli: 8
Wheezing : 1

OrderedDict([('Severity Level', 6.4629)])
```



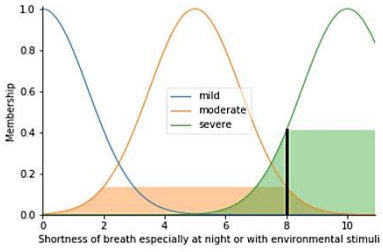
Output = 6.463

Figure 16: Asthma severity level by applying triangular membership function.

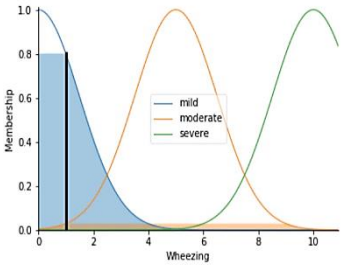
For the same inputs stated above, the system has given the severity level of asthma to be 7.415 while applying gaussian membership function.



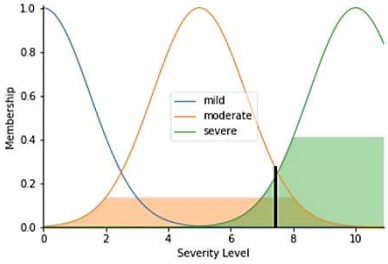
Input 1 = 7



Input 2 = 8




```
Cough_at_night_or_with_environmental_stimuli: 7
Shortness_of_breath_especialy_at_night_or_with_
environmental_stimuli: 8
Wheezing : 1

OrderedDict([('Severity Level', 7.4146)])
```



Output = 7.415

Figure 17: Asthma severity level by applying gaussian membership function.

According to the knowledge gathered from the three doctors, among the three symptoms of asthma, severity range of shortness of breath especially at night or with environmental stimuli mainly helps to decide the severity of the asthma disease that one has. Having that in mind, by giving the same least value (1) to the two symptoms (cough and wheezing) and by varying the severity level of shortness of breath, comparison was made to the outputs of the two membership functions. The final results are shown in table 6. The result obtained by the triangular membership function was found acceptable by the experts. Therefore, the triangular membership function was applied to design the fuzzy expert system.

Table 6: Comparison between triangular and gaussian membership functions on asthma severity level prediction.

No	Asthma symptom-1: Cough at night or with environmental stimuli	Asthma symptom-2: Shortness of breath especially at night or with environmental stimuli	Asthma symptom-3: Wheezing	Severity level of Asthma by using triangular membership function	Severity level of Asthma by using gaussian membership function
1	1	1	1	**1.7**	**1.69**
2	1	2	1	**3.365**	**3.20**
3	1	3	1	**4.2**	**4.691**
4	1	4	1	**4.687**	**4.981**
5	1	5	1	**5.00**	**5.01**
6	1	6	1	**5.3127**	**5.06**
7	1	7	1	**5.79**	**5.55**
8	1	8	1	**6.634**	**7.41**
9	1	9	1	**8.27**	**8.90**
10	1	10	1	**8.27**	**9.19**

As shown in table 4 and 5, the triangular ranges were not the same for all the linguistic variables; so three different triangular membership functions were formulated as presented in table 7, 8 and 9. These formulas were determined with the aid of both expert doctors and literatures.

The triangular membership function is expressed with the following equation:

$$\mu_A(x) = \begin{cases} 0 & if \quad x < a \\ \frac{x-a}{b-a} & if \quad a \leq x \leq b \\ \frac{c-x}{c-b} & if \quad b < x \leq c \\ 0 & if \quad x > c \end{cases}$$

Where: a, b, c – are fuzzy triangular parameters and
A – is linguistic variable

Range of Fuzzy value 1

Table 7: Range of fuzzy values between 0 and 10.

Linguistic Variables	Fuzzy Values for the range of (0 - 10)
Mild	$0 \leq x \leq 5$
Moderate	$1 \leq x \leq 9$
Severe	$5 \leq x \leq 10$

$$\mu_{Mild}(x) = \begin{cases} 0 & if \quad x < 0 \\ \frac{5-x}{5} & if \quad 0 < x \leq 5 \\ 0 & if \quad x > 5 \end{cases}$$

Where a = 0, b = 0 and c = 5

$$\mu_{Moderate}(x) = \begin{cases} 0 & if \quad x < 1 \\ \frac{x-1}{4} & if \quad 1 \leq x \leq 5 \\ \frac{9-x}{4} & if \quad 5 < x \leq 9 \\ 0 & if \quad x > 9 \end{cases}$$

Where a = 1, b = 5 and c = 9

$$\mu_{Severe}(x) = \begin{cases} 0 & if \quad x < 5 \\ \frac{X-5}{5} & if \quad 5 \leq x \leq 10 \\ 0 & if \quad x > 10 \end{cases}$$

Where a = 5, b = 10 and c = 10

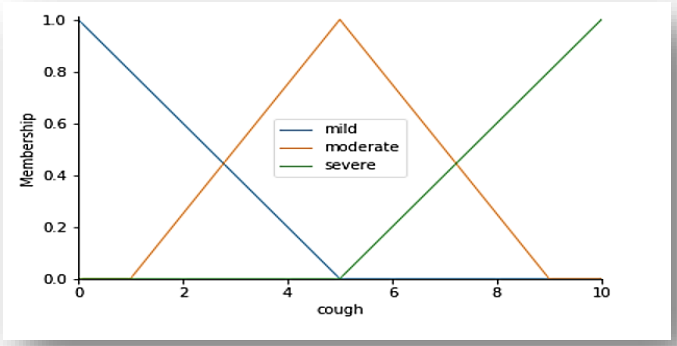


Figure 18: Membership graph of fuzzy variable cough having range of 0 – 10.

Range of fuzzy values 2

Table 8: Range of fuzzy values between 17 and 35.

Linguistic Variables	Fuzzy Values for the range of (17 - 35)
Mild	$17 \leq x \leq 26$
Moderate	$18 \leq x \leq 34$
Severe	$26 \leq x \leq 35$

$$\mu_{Mild}(x) = \begin{cases} 0 & if \quad x < 17 \\ \frac{26-x}{9} & if \quad 17 < x \leq 26 \\ 0 & if \quad x > 26 \end{cases}$$

Where a = 17, b = 17 and c = 26

$$\mu_{Moderate}(x) = \begin{cases} 0 & if \quad x < 18 \\ \frac{x-18}{8} & if \quad 18 \leq x \leq 26 \\ \frac{34-x}{8} & if \quad 26 < x \leq 34 \\ 0 & if \quad x > 34 \end{cases}$$

Where a = 18, b = 26 and c = 34

$$\mu_{Severe}(x) = \begin{cases} 0 & if \quad x < 26 \\ \frac{x-26}{9} & if \quad 26 \leq x \leq 35 \\ 0 & if \quad x > 35 \end{cases}$$

Where a = 26, b = 35 and c = 35

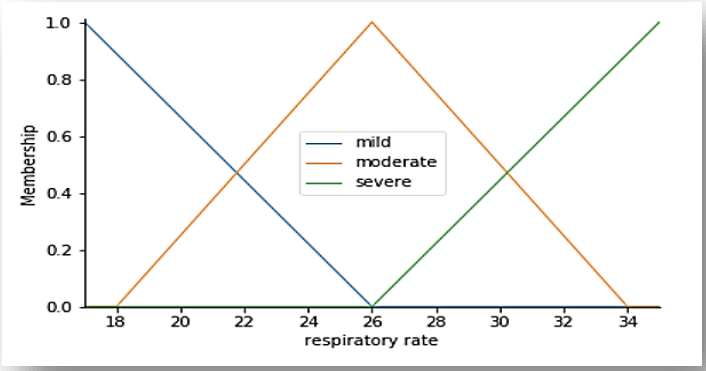


Figure 19: Membership graph of fuzzy variable respiratory rate having range.

Range of fuzzy values 3

Table 9: Range of fuzzy values between 0 and 20.

Linguistic Variables	Fuzzy Values for the range of (0 - 20)
Mild	$0 \leq x \leq 10$
Moderate	$1 \leq x \leq 19$
Severe	$10 \leq x \leq 20$

$$\mu_{Mild}(x) = \begin{cases} 0 & if \quad x < 0 \\ \dfrac{10 - x}{10} & if \quad 0 < x \leq 10 \\ 0 & if \quad x > 10 \end{cases}$$

Where a = 0, b = 0 and c = 10

$$\mu_{Moderate}(x) = \begin{cases} 0 & if \quad x < 1 \\ \dfrac{x - 1}{9} & if \quad 1 \leq x \leq 10 \\ \dfrac{19 - x}{9} & if \quad 10 < x \leq 19 \\ 0 & if \quad x > 19 \end{cases}$$

Where a = 1, b = 10 and c = 19

$$\mu_{Severe}(x) = \begin{cases} 0 & if \quad x < 10 \\ \dfrac{x - 10}{10} & if \quad 10 \leq x \leq 20 \\ 0 & if \quad x > 20 \end{cases}$$

Where a = 10, b = 20 and c = 20

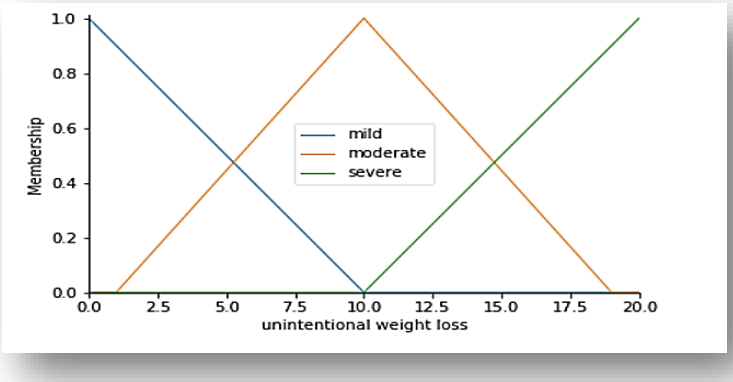


Figure 20: Membership graph of fuzzy variable unintentional weight loss having range.

The next step is developing the fuzzy rules with the help of the domain experts (three medical doctors). Based on the experts' knowledge and experience, rules were formulated for PTB, pneumonia, asthma, COPD and the four extra-pulmonary diseases namely: TB of GIT, TB of lymph-node, TB of osteo-articular and TB of meninges. In order to make the rules more universal, different diagnostic guidelines were also considered by the experts. For example, there is a guide for pneumonia diagnosis saying that patients with 2 or more of the specified pneumonia symptoms were to take examinations to confirm their case. Examples of some of the rules used for PTB are shown in table 10.

Table 10: Fuzzy Rule Base example for PTB.

R. No	**For PTB**					
	Cough	**Unintentional weight loss**	**Breathing rate**	**Chest pain or tightness**	**Shortness of Breath**	**Conclusion**
1	Mild	Mild	Mild	Mild	Mild	Mild
2	Mild	Moderate	Mild	Mild	Mild	Mild
5	Mild	Mild	Mild	Moderate	Mild	Moderate
6	Mild	Mild	Mild	Mild	Moderate	Moderate
7	Moderate	Moderate	Mild	Mild	Mild	Moderate
10	Moderate	Mild	Mild	Mild	Moderate	Moderate
17	Moderate	Moderate	Moderate	Mild	Mild	Moderate
22	Moderate	Mild	Moderate	Mild	Moderate	Moderate
26	Mild	Mild	Moderate	Moderate	Moderate	Moderate
27	Moderate	Moderate	Moderate	Moderate	Mild	Moderate
32	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
33	Severe	Moderate	Moderate	Moderate	Moderate	Severe
40	Moderate	Severe	Mild	Moderate	Moderate	Severe
49	Moderate	Moderate	Severe	Moderate	Mild	Severe
55	Moderate	Moderate	Moderate	Severe	Mild	Severe
63	Severe	Severe	Moderate	Moderate	Moderate	Severe
65	Severe	Moderate	Moderate	Severe	Moderate	Severe
73	Severe	Severe	Moderate	Moderate	Mild	Severe

79	Severe	Moderate	Severe	Mild	Moderate	Severe
97	Mild	Severe	Severe	Moderate	Moderate	Severe
101	Moderate	Severe	Severe	Mild	Moderate	Severe
115	Moderate	Moderate	Severe	Severe	Mild	Severe
127	Moderate	Mild	Moderate	Severe	Severe	Severe
133	Severe	Severe	Severe	Moderate	Moderate	Severe
134	Severe	Moderate	Severe	Severe	Moderate	Severe
136	Moderate	Severe	Severe	Severe	Moderate	Severe
139	Severe	Severe	Moderate	Severe	Moderate	Severe
146	Moderate	Severe	Severe	Severe	Mild	Severe
157	Moderate	Severe	Mild	Severe	Severe	Severe
172	Mild	Severe	Severe	Severe	Severe	Severe
173	Severe	Severe	Severe	Severe	Severe	Severe

Some of the rules can be interpreted as follows:

Rule1: IF cough = mild and unintentional weight loss = mild and breathing rate = mild and chest pain or tightness = mild and shortness of breath = mild THEN PTB = mild.

Rule2: IF cough = mild and unintentional weight loss = moderate and breathing rate = mild and chest pain or tightness = mild and shortness of breath = mild THEN PTB = mild.

Rule5: IF cough = mild and unintentional weight loss = mild and breathing rate = mild and chest pain or tightness = moderate and shortness of breath = mild THEN PTB = moderate.

Rule6: IF cough = mild and unintentional weight loss = mild and breathing rate = mild and chest pain or tightness = mild and shortness of breath = moderate THEN PTB = moderate

Rule32: IF cough = moderate and unintentional weight loss = moderate and breathing rate = moderate and chest pain or tightness = moderate and shortness of breath = moderate THEN PTB = moderate.

Rule33: IF cough = severe and unintentional weight loss = moderate and breathing rate = moderate and chest pain or tightness = moderate and shortness of breath = moderate THEN PTB = severe.

Rule67: IF cough = moderate and unintentional weight loss = severe and breathing rate = severe and chest pain or tightness = moderate and shortness of breath = moderate THEN PTB = severe.

Rule133: IF cough = severe and unintentional weight loss = severe and breathing rate = severe and chest pain or tightness = moderate and shortness of breath = moderate THEN PTB = severe.

Rule172: IF cough = mild and unintentional weight loss = severe and breathing rate = severe and chest pain or tightness = severe and shortness of breath = severe THEN PTB = severe.

Rule173: IF cough = severe and unintentional weight loss = severe and breathing rate = severe and chest pain or tightness = severe and shortness of breath = severe THEN PTB = severe.

The rules formulated in the thesis use fuzzy logic operator AND to combine the fuzzy values of the antecedent part and takes the minimum of all. This will be explained in brief in the next section. A rule is said to fire if the minimum value from the fuzzy values in the antecedent part (mild, moderate, severe) evaluates to true (1 or > 0); otherwise, if all the parameters evaluate to false (0), it does not fire.

IV. Fuzzy inference

In fuzzy expert systems, fuzzy inference is the key component. It is being applied in so many fields where decisional support is needed. Its success is mainly because it relates to human reasoning capability.

As mentioned in the introduction section, there are three types of fuzzy inference methods: mamdani, sugeno and tsukamoto fuzzy inference. These three methods can be divided into two processes. The first process is fuzzifying the crisp values for which all the three methods are exactly the same. The difference occurs when the aggregated fuzzy value is converted to a crisp output [33].

In mamdani inference method, the consequent part of each rule is a fuzzy set and defuzzification is applied on the aggregated output of each of the rules. In sugeno inference mechanism, complex method of defuzzification is avoided. “The work of determining the parameters of polynomials is inefficient and less straightforward than defining the output fuzzy sets for mamdani inference” [33].

On the other hand, in tsukamoto inference mechanism, the consequent of each fuzzy rule is represented by a fuzzy set with a monotonically increasing or decreasing membership function unlike the other two methods. As a result, the inferred output of each rule is a crisp value corresponding to the firing strength of the rules. The overall output is taken as the weighted average of the output of each rule [33].

It is more efficient to use a single spike as the output membership function rather than a distributed fuzzy set, thus enabling the output to be easily understood by the end user. Due to the above reasons mamdani fuzzy inference method was chosen for the current thesis work.

Mamdani fuzzy inference method

Mamdani method of inference, which is the main focus of this research, was proposed as the first attempt to solve control problems by a set of linguistic rules obtained from experienced human operators [64]. "In mamdani fuzzy systems, both antecedent and consequent are linguistic terms and the output corresponds to the superposition of individual outputs given by each rule" [65].

There are five steps in the mamdani fuzzy inference method (see also figure 21):

Step 1: Fuzzify input variables – which is discussed in the previous section

Step 2: Apply fuzzy operator

Step 3: Apply implication method

Step 4: Apply aggregation method

Step 5: Defuzzification

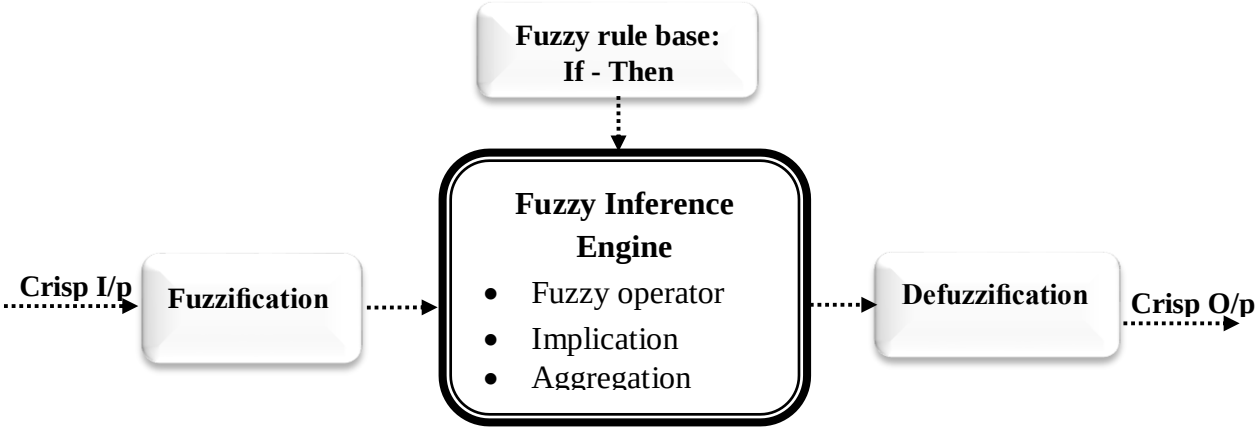


Figure 21: Major components of mamdani-type fuzzy inference process [64].

The knowledge base with all the fuzzy rules and the fuzzification process was discussed above; therefore, the rest of mamdani inference processes, which are the inference engine and the deffuzification processes, will be explained next.

- **Appling fuzzy logic operators**

In order to find a single value which will represent the result of the antecedent part of a rule, an operator which combines membership values is required. There are two fuzzy logic operators which are well-known for their simplicity and effectiveness. These operators are AND and OR. These logic operators are formulated by min and max functions respectively. As shown in figure 22, one of the two most common logical operator which is AND has been used in the current thesis [33].

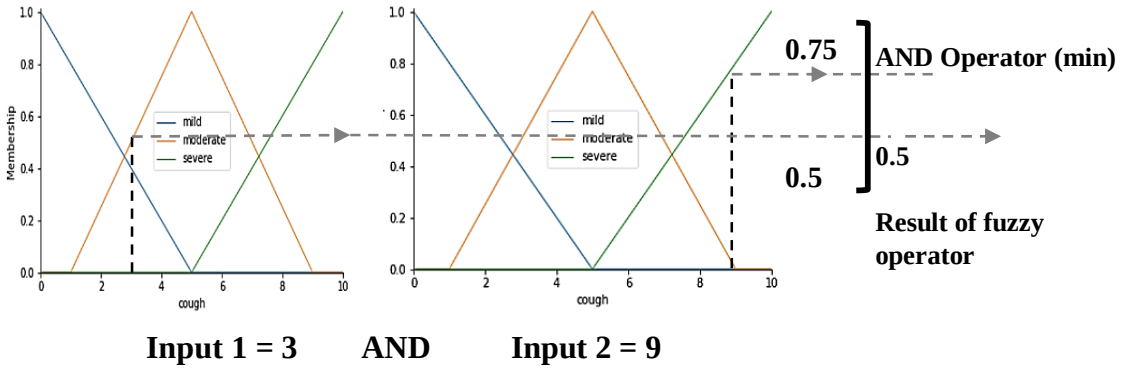


Figure 22: Using fuzzy logic operator AND to combine two inputs in the designed fuzzy system.

As mentioned above, the fuzzy operator AND will be applied to each rule in order to combine the antecedent's value and obtain one fuzzy number which is the minimum of all.

- **Implication method**

In the inference method, the result obtained when applying fuzzy logic operator on the antecedent part of each rule is a single value. This value is reshaped to give the exact result as a consequent by using the implication method [33].

$$A_i = I_1 \Lambda I_2 \Lambda I_3 \dots I_i$$

Where – A_i is the matching degree of a given input which *s*atisfies the condition of the i^{th} rule and $i = 1, 2..$

– I_1, I_2, $I_3 \dots I_i$ are the fuzzy input values in the antecedent part of the i^{th} rule and $i = 1, 2..$

When applying the implication method as shown in figure 23, the A_i which is obtained by combining the input values in the antecedent part with fuzzy logic operator AND, is assigned to the rule's consequent part C_i as; $A_i = C_i$, where - C_i is the consequent part of the i^{th} rule

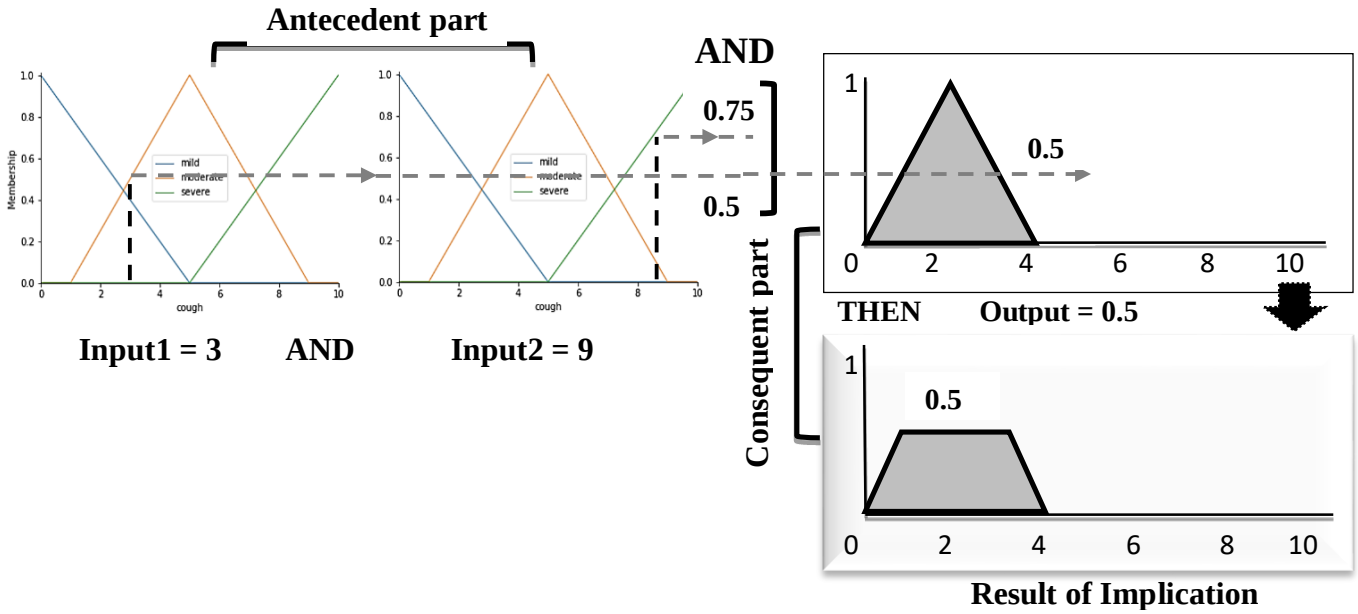


Figure 23: Implication process in the designed fuzzy system.

- **Aggregation method**

Aggregation is the process of combining fuzzy sets that represent the outputs of all rules into a single fuzzy set. It takes the output of the implication process, which is a list of truncated output functions of all the rules, and combines them to give a single fuzzy set for each output variable in order to make a decision [29].

There are three methods used to aggregate rules in a fuzzy logic expert system: max (maximum), probor (probabilistic or) and sum (sum of the rule output sets). Since aggregation method is commutative, execution order of the rules in the knowledge base is not important.

In this thesis, maximum method of aggregation was used as shown in figure 24. The choice of the maximum method of aggregation was made with the help of the doctors.

Input one (Cough) = Moderate – 6 out of 10, Input two (Wheezing) = Severe – 9 out of 10

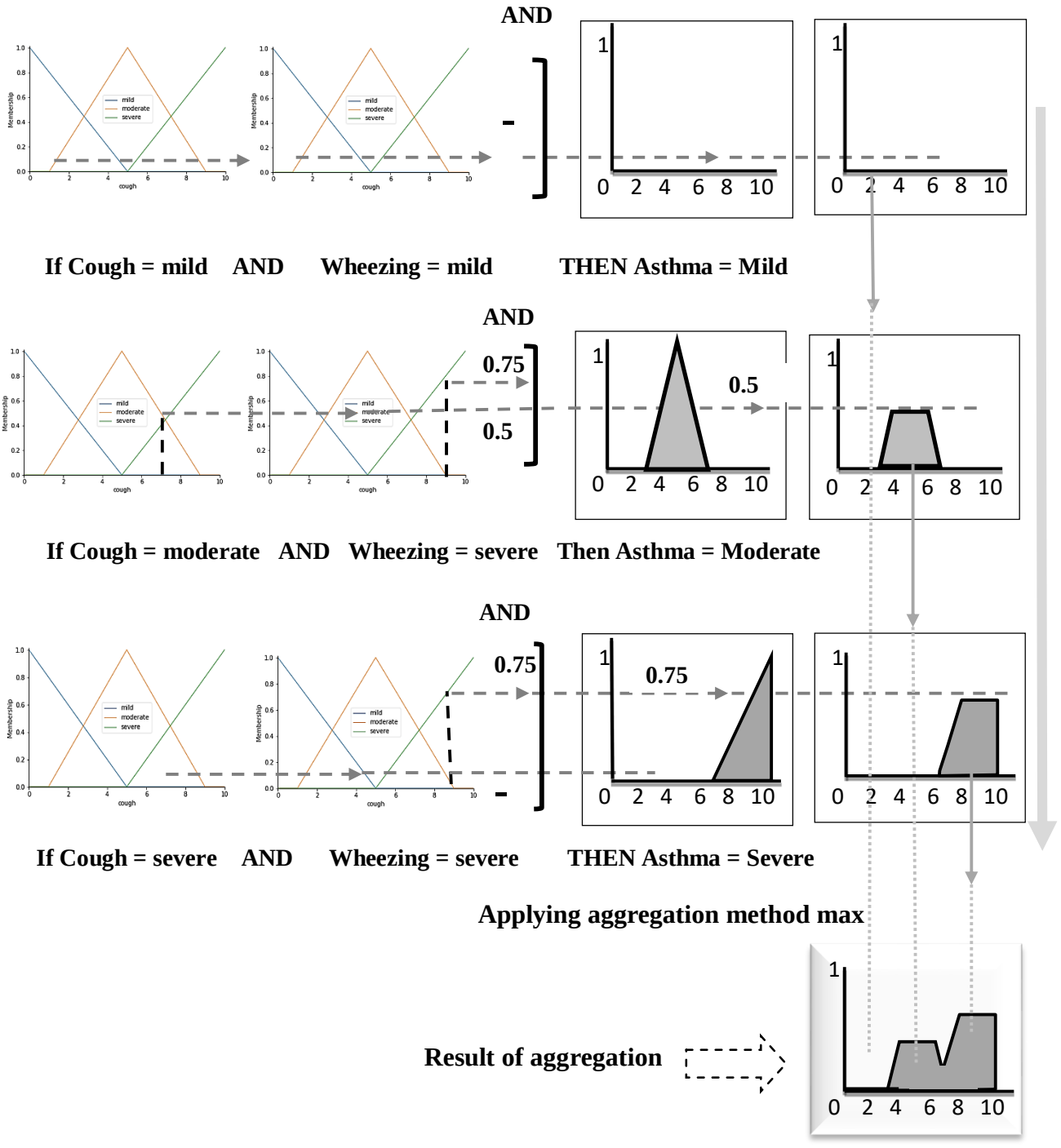


Figure 24: The aggregation process in the designed fuzzy system.

- **Defuzzification**

Once the aggregated output has been found, the next step is the defuzzification process. Defuzzification is a very essential process in fuzzy expert systems. The output of the aggregation process is a single fuzzy set. This fuzzy set cannot be understood by the user if it was to be presented as the output. Therefore, to make the final output understandable for the user, the output of the aggregation process needs to be defuzzified to a crisp value.

Among the six defuzzification methods mentioned in the introduction section, centroid method was used in this thesis.

The choice of centroid method among the different methods of defuzzification was done by reviewing different literatures and evaluating the output of the most common methods of defuzzification. Different literatures have made comparisons between different methods of defuzzification based on the consistency in their output and performance [66], [67]. They recommended the use of COG for fuzzy logic applications. COG has proven its simplicity and efficiency by providing a consistent and acceptable output by the domain experts in comparison to other methods of defuzzification in this research. Comparison between different methods of defuzzification is shown in figure 25 and table 11.

The centroid or Center of Gravity (COG) method of diffuzification is expressed by the following equation [38]:

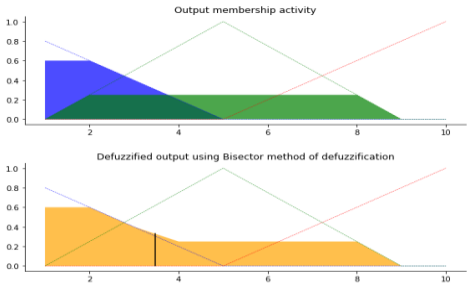
$$\boldsymbol{COG(Y')} = \frac{\sum \boldsymbol{\mu_Y(X_i)X_i}}{\sum \boldsymbol{\mu_Y(X_i)}}$$

Where $\boldsymbol{\mu_Y(X_i)}$ = Membership value in the membership function and

$\boldsymbol{X_i}$ = Center of membership function

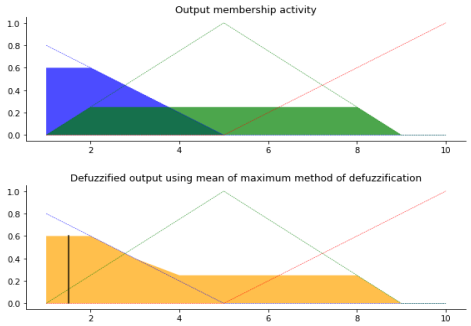
By using bisector method of defuzifiation

```
Cough_at_night_or_with_environmental_
stimuli: 1
Shortness_of_breath_especialy_at_
night_or_with environmental_stimuli: 2
Wheezing : 1

Severity level of Asthma is 3.4808
```



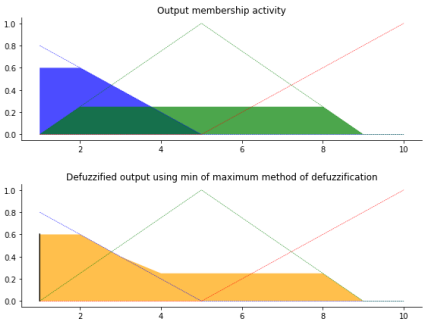
By using mean of maximum method of defuzifiation

```
Cough_at_night_or_with_environmental_
stimuli: 1

Shortness_of_breath_especialy_at_
night_or_with environmental_stimuli: 2
Wheezing : 1

Severity level of Asthma is 1.5
```



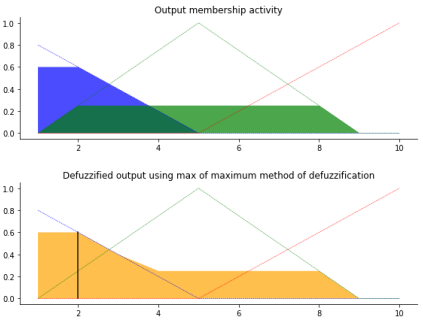
By using min of maximum method of defuzifiation

```
Cough_at_night_or_with_environmental_
stimuli: 1
Shortness_of_breath_especialy_at_
night_or_with environmental_stimuli: 2
Wheezing : 1

Severity level of Asthma is 1.0
```



By using max of maximum method of defuzifiation

```
Cough_at_night_or_with_environmental_
stimuli: 1

Shortness_of_breath_especialy_at_
night_or_with environmental_stimuli: 2
Wheezing : 1

Severity level of Asthma is 2.0
```



By using center of gravity method of defuzifiation

```
Cough_at_night_or_with_environmental_
stimuli: 1
Shortness_of_breath_especialy_at_
night_or_with environmental_stimuli: 2
Wheezing : 1

Severity level of Asthma is 3.3651
```

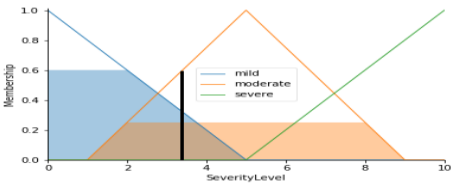


Figure 25: Output of different methods of defuzzification in the diagnosis of Asthma provided the same input.

Table 11: Comparison of different methods of defuzification in the diagnosis of Asthma.

No	Asthma symptom-1: Cough at night or with environmental stimuli	Asthma symptom-2: Shortness of breath especially at night or with environmental stimuli	Asthma symptom-3: Wheezing	Severity level of Asthma by using bisector method of defuzzification	Severity level of Asthma by using mean of maximum method of defuzzification	Severity level of Asthma by using min of maximum method of defuzzification	Severity level of Asthma by using max of maximum method of defuzzification	Severity level of Asthma by using center of gravity method of defuzzification
1	1	1	1	2.17	1.0	1.0	1	**1.7**
2	1	2	1	3.480	1.5	1.0	2	**3.365**
3	1	3	1	4.65	5.0	3.0	7	**4.2**
4	1	4	1	4.933	5.0	4.0	6	**4.687**
5	1	5	1	5.0	5.0	5.0	5	**5.00**
6	1	6	1	5.2	5.0	4.0	6	**5.3127**
7	1	7	1	5.75	5.0	3.0	7	**5.79**
8	1	8	1	7.29	9.0	8.0	10	**6.634**
9	1	9	1	8.46	9.5	9.0	10	**8.27**
10	1	10	1	8.46	9.5	9.0	10	**8.27**

As the comparison made for choosing the suitable membership function that is shown in table 6, by giving the same least value (1) to the two symptoms (cough and wheezing) of asthma and by varying the severity level of shortness of breath, comparison was also made to the outputs of the five main methods of defuzzification as shown in table 11.The result obtained by the center of gravity defuzzification method was acceptable by the experts. Therefore, center of gravity defuzzification method was applied to design the fuzzy expert system as shown in figure 26.

Input one (Cough) = Moderate – 6 out of 10, Input two (Wheezing) = Severe – 9 out of 10

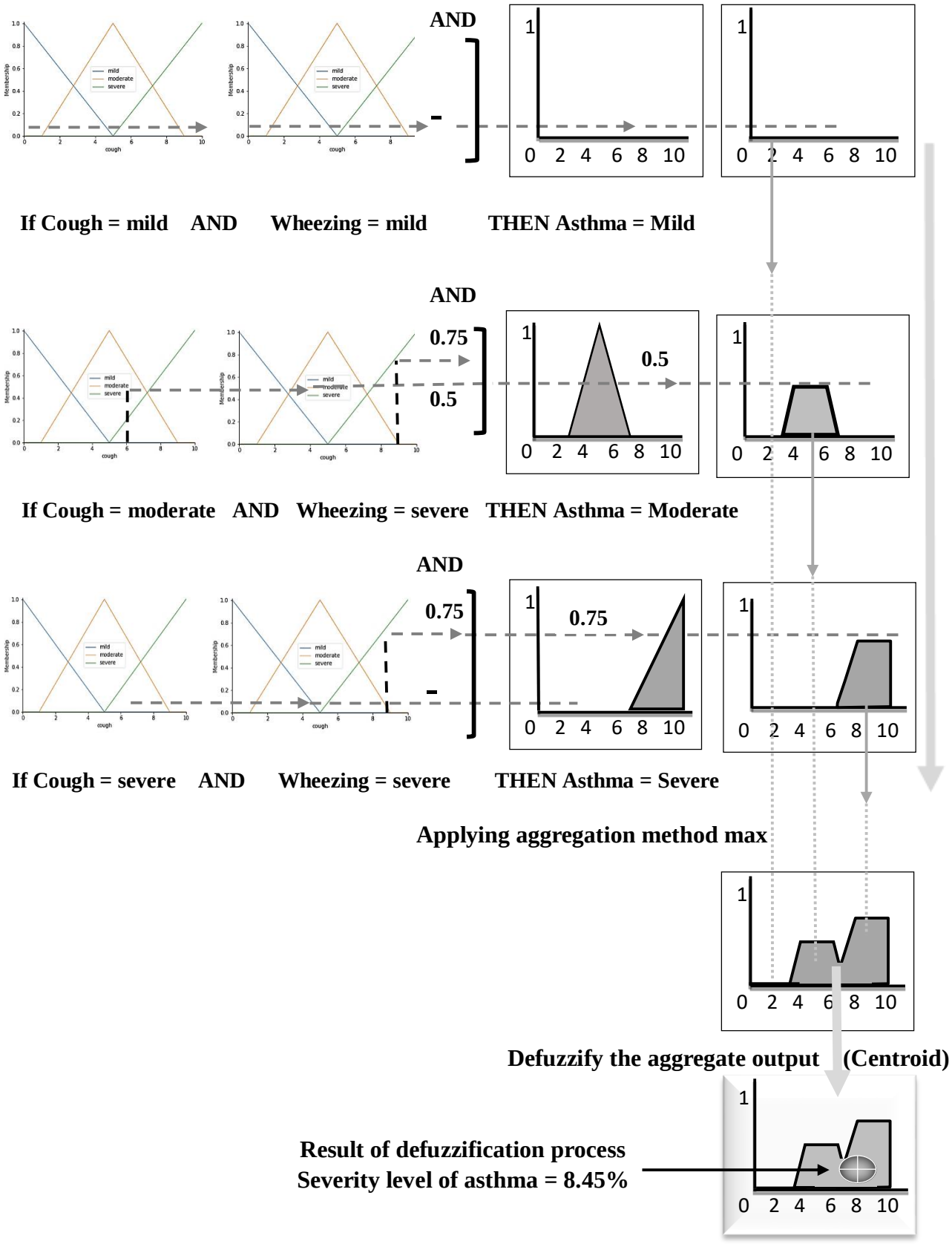
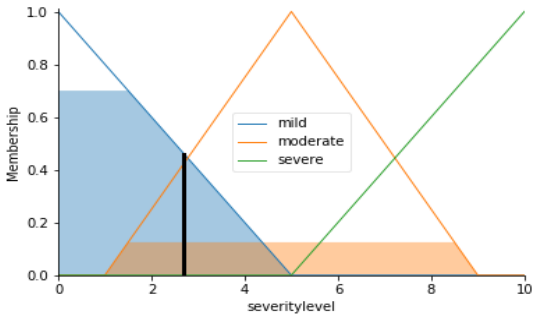


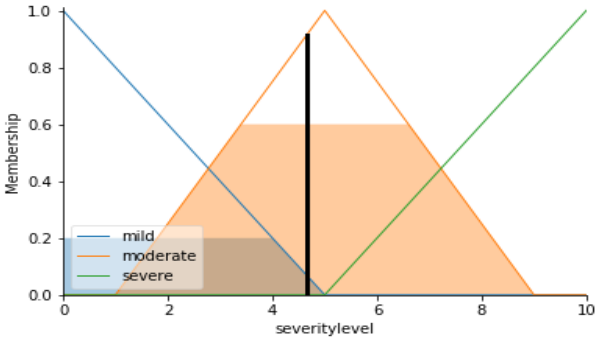
Figure 26: The defuzzification process in the designed fuzzy system.

A simulation of the fuzzy expert system for the diagnosis of PTB with varying inputs is shown in figure 27.

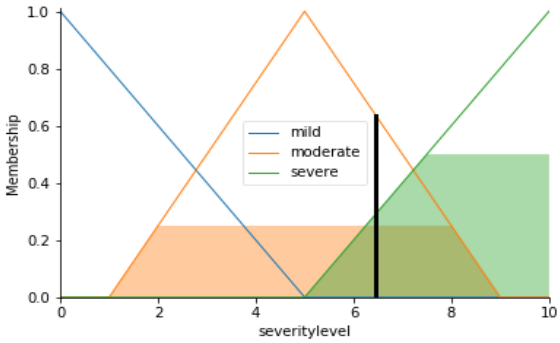
```
cough : 1
unintentional_weight_loss : 3
respiratory_rate : 19
chest_pain_or_tightness : 1
shortness_of_breath : 1

Severity level of PTB is: 2.6974
Suspicion level for PTB is Mild
```




```
cough : 4
unintentional_weight_loss : 1
respiratory_rate : 20
chest_pain_or_tightness : 2
shortness_of_breath : 1

Severity level of PTB is: 4.6539
Suspicion level of PTB is Moderate,
  further diagnosis is recommended
```




```
cough : 3
unintentional_weight_loss : 2
respiratory_rate : 30
chest_pain_or_tightness : 5
shortness_of_breath : 8

Severity level of PTB is: 6.4629
Suspicion level for PTB is Moderate,
  further diagnosis is recommended
```




```
cough : 2
unintentional_weight_loss : 1
respiratory_rate : 32
chest_pain_or_tightness : 9
shortness_of_breath : 4

Severity level of PTB is: 8.1428
Suspicion level for PTB is
  slightly Severe, further diagnosis
  is highly recommended
```

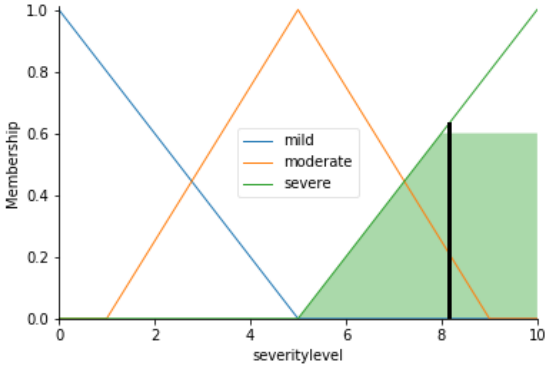


Figure 27: The fuzzy expert system PTB diagnosis output for varying patient symptoms (inputs).

3.7.2 The rule based expert system design

After laboratory and radiology tests were conducted and fed to the system, the examination assessment was done using a rule based expert system. Unlike symptoms, which can be ambiguous and imprecise, diagnostic examinations are reliable if the proper test is ordered and the diagnostic equipment functionality is not in question. Therefore, instead of the fuzzy system which deals with imprecision, rule based expert system was chosen.

Architecture of the rule based expert system design

The core components of the systems are the knowledge base and the reasoning engine as shown in figure 28.

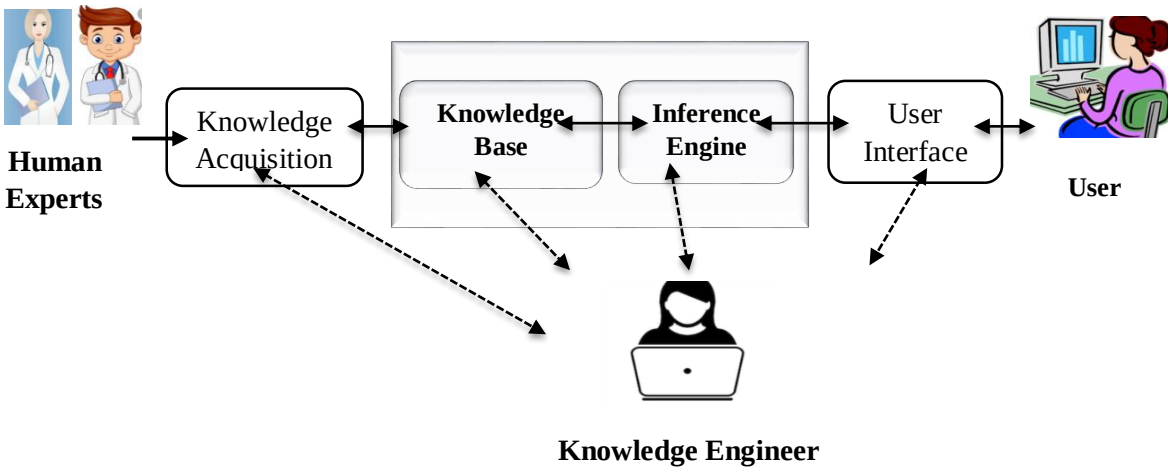


Figure 28: Architecture of the designed rule based expert system.

I. Knowledge acquisition

To acquire a general knowledge about the types of examinations used for the diagnosis of pulmonary and extra-pulmonary TB, different secondary sources of data were used such as TB diagnosis and treatment guideline of Ethiopia and WHO.

Once some hint was obtained, a form shown in table 28 was prepared to be filled by the three doctors and laboratory technicians working in the study areas. The form contains a list of examinations from the guidelines.

The physicians were expected to mark those examinations which they order in their day to day diagnosis procedure and add other examinations which need to be added to the list. The form was prepared with the intention of saving the health professionals' precious time.

This procedure of selecting the examination for PTB and the four chosen EPTBs is briefly explained in the data analysis section. In table 12, the chosen examination modalities for each of the 5 diseases are presented.

The acquired knowledge was organized and saved in the knowledge base in the form of IF-THEN rules.

Table 12: The selected examination modalities for PTB and the four chosen EPTB diseases.

No	List of Examinations for PTB	List of Examinations for TB of Meninges	List of Examinations for TB of Lymph-node	List of Examinations for TB of Osteo-articular	List of Examinations for TB of GIT
1	ESR finding	CSF Finding for WBC	FNAC Finding	MRI Finding of the Affected Area	Abdominal Ultrasound
2	Chest X-ray finding	CSF Finding for Protein	Lymph-node biopsy	XR Finding of the Affected Area	CT of Abdomen
3	GeneXpert finding	CSF Finding for Glucose		Finding of Synovial Fluid Aspiration	Ascetic fluid Analysis
4	HIV test	CT of Brain Finding		Biopsy Finding	Histopathology finding

II. The knowledge base

The combinations of examination findings for each disease were presented in a table format. An example for PTB is shown in table 13.

Table 13: The possible combination of examination findings for the diagnosis of PTB.

Rule No	IF Erythrocyte Sedimenta-tion rate Finding	& Finding of Gene expert Analysis	& Chest X-ray Finding	& HIV Test Finding	THEN Diagnostic result
1	Normal	Bacteria not detected	Not Suggestive of PTB	Negative for HIV	Negative for PTB
2	Suggestive of Chronic illness	Bacteria not detected	Not Suggestive of PTB	Negative for HIV	Negative for PTB

3	Normal	Presence of bacteria detected	Not Suggestive of PTB	Negative for HIV	Positive for PTB
4	Normal	Bacteria not detected	Suggestive of PTB	Negative for HIV	Positive for PTB
5	Normal	Bacteria not detected	Not Suggestive of PTB	Positive for HIV	Negative for PTB
6	Suggestive of Chronic illness	Presence of bacteria detected	Not Suggestive of PTB	Negative for HIV	Positive for PTB
7	Suggestive of Chronic illness	Bacteria not detected	Suggestive of PTB	Negative for HIV	Positive for PTB
8	Suggestive of Chronic illness	Bacteria not detected	Not Suggestive of PTB	Positive for HIV	Negative for PTB
9	Normal	Presence of bacteria detected	Suggestive of PTB	Negative for HIV	Positive for PTB
10	Normal	Presence of bacteria detected	Not Suggestive of PTB	Positive for HIV	Positive for PTB
11	Normal	Bacteria not detected	Suggestive of PTB	Positive for HIV	Positive for PTB
12	Suggestive of Chronic illness	Presence of bacteria detected	Suggestive of PTB	Negative for HIV	Positive for PTB
13	Suggestive of Chronic illness	Presence of bacteria detected	Not Suggestive of PTB	Positive for HIV	Positive for PTB
14	Suggestive of Chronic illness	Bacteria not detected	Suggestive of PTB	Positive for HIV	Positive for PTB
15	Normal	Presence of bacteria detected	Suggestive of PTB	Positive for HIV	Positive for PTB
16	Suggestive of Chronic illness	Presence of bacteria detected	Suggestive of PTB	Positive for HIV	Positive for PTB

The data is then converted to IF-THEN rules to be saved in the knowledge base. The inference engine refers to the knowledge base to pass decision.

Sample of rules for table 13 are shown below:

Rule1: if Erythrocyte_sedimentation_rate_finding = "Normal" and Finding_of_gene_expert_analysis = "Bacteria not detected" and Chest_Xray_finding = "Not suggestive of PTB" and HIV_test_finding = "Negative for HIV" THEN diagnosis= "Negative for PTB"

Rule2: elif Erythrocyte_sedimentation_rate_finding = "Suggestive of chronic illness" and Finding_of_gene_expert_analysis = "Bacteria not detected" and Chest_Xray_finding = "Not suggestive of PTB" and HIV_test_finding = "Negative for HIV" THEN diagnosis= "Negative for PTB"

Rule9: elif Erythrocyte_sedimentation_rate_finding = "Normal" and Finding_of_gene_expert_analysis = "Presence of bacteria detected" and Chest_Xray_finding = "Suggestive of PTB" and HIV_test_finding = "Negative for HIV" THEN diagnosis = "Positive for PTB"

Rule10: elif Erythrocyte_sedimentation_rate_finding = "Normal" and Finding_of_gene_expert_analysis = "Presence of bacteria detected" and Chest_Xray_finding = "Not suggestive of PTB" and HIV_test_finding = "Positive for HIV" THEN diagnosis= "Positive for PTB"

IV. Inference engine

The inference engine analyses and processes the rules to arrive at a conclusion. In this research, the final diagnosis result is achieved by analysing the input examination findings. Therefore, from the two strategies of inference engine, forward chaining was applied to reach at the diagnostic conclusion.

The logic operator AND was used to connect different examinations to find the final diagnosis result. Application of the forward chain for examination finding analysis is shown in figure 29.

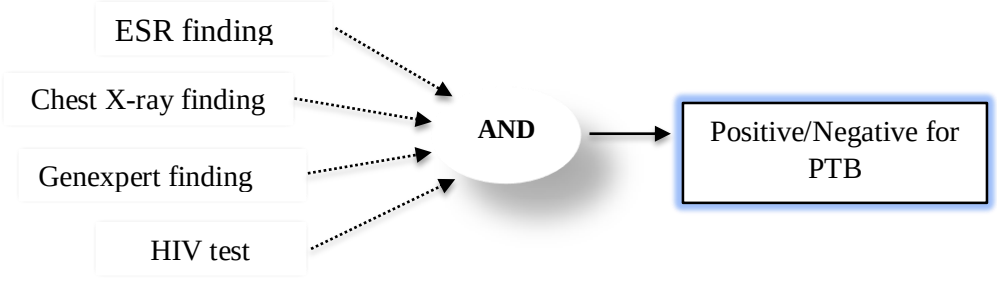


Figure 29: Forward chaining example of PTB diagnosis used in the designed rule based expert system.

V. User

The user may or may not be an expert in the specific area on which the system is designed for. When considering the user with the least knowhow, they just need to be a health-care professional (nurse) with some knowledge about TB and with some training on how to use the system properly and efficiently.

3.8 TB medication prescription

After the system runs both the fuzzy and rule based diagnosis and the final result is acquired, medication prescription, dosage and few recommendations which are saved in the database will be displayed to the user. The generalized medication for each disease in the designed system which is forwarded from the data analysis section, and few recommendations which needed to be followed are discussed next.

Treatment of tuberculosis

The treatment of TB takes much longer than treating other types of bacterial infections. For active tuberculosis, a patient must take antibiotics for at least six to nine months or more in some cases. Doctors working in the area agree that "the exact drugs and length of treatment depend on age, overall health, possible drug resistance and the infection's location in the body" [8], [68].

TB treatment regimens

The drugs used for TB treatment are safe and effective if properly used. The drugs shown in table 14 with their respective dosage according to patient's weight are the ones used as first line treatments of TB in Ethiopia and in many countries as indicated by WHO guideline [8], [68]:

Table 14: First-line anti-TB drugs and their recommended dosages based on patient's weight [8], [68].

Drug	Dose and range (mg/kg body weight)	Maximum dose per day
Isoniazid, H	5 (4-6)	300 mg/day
Rifampicin, R	10 (8-12)	600 mg/day
Pyrazinamide, Z	25 (20-30)	2000 mg/day
Ethambutol, E	15(15-20)	1500 mg/day
Streptomycin, S	15 (12-18)	1 gm/day

- **Fixed-dose combinations of anti-TB drugs**

As indicated in table 14, the regimen used shows combination of first line TB drugs which is called Fixed-Dose Combinations (FDCs). The drugs available in FDC are [68]:

- Rifampicin, Isoniazid, Pyrazinamide and Ethambutol (RHZE 150/75/400/275 mg)
- Rifampicin and Isoniazid (RH 150/75 mg)
- Ethambutol and Isoniazid (EH 400/150 mg)

FDCs of anti-TB drugs are introduced to prevent patients from developing drug resistant TB which may occur with separate drugs (mono-therapy). Since FDCs [68]:

- Prevent the patient from being selective in choosing from the four drugs
- Reduce error caused during medication prescription
- Make it easier to adjust medication dosage based on patient's weight
- Decrease the number of tablets to be ingested, which encourages patients to finish the regimen

Number of tablets of four fixed combination doses and two fixed combination doses per day for adults and children weighing ≥ 25kg is shown in table 15.

Table 15: Number of tablets of fixed combination doses [8], [68].

Pre-treatment body weight	**Intensive Phase 7 days a week for 2 months**	**Continuation phase 7 days a week for 4 months**	
	RHZE (150 mg,75 mg, 400 mg,275 mg)	RH (150 mg,75 mg)	RH (300 mg,150 mg)
Children weighing ≥ 25kg	2 tabs	2 tabs	
30-37 kg	2 tabs	2 tabs	
38-54 kg	3 tabs	3 tabs	
55-70 kg	4 tabs	4 tabs	2 tabs
>70kg	5 tabs	4 tabs	2 tabs

Monitoring the treatment response

A number of measures are monitored to determine response to treatment. These includes physical signs such as reduced symptoms, weight gain, increased appetite and improvement in strength and check-ups are recommended to be done on monthly basis but if not possible, they must be done [69]:

- At the end of intensive phase
- At end of the fifth month and
- At the end of treatment

After the end of the intensive phase, greater than 80%, and as the treatment proceeds to third month, greater than 90% of smear positive cases should be smear negative. This improvement of smear finding is a major indication that the treatment is working. The same thing applies for extra-pulmonary TB, the biopsy should indicate negative results as the treatment proceeds [69].

3.9 Chest X-ray image classification of the system

3.9.1 The dataset

The Dataset used was from “China Set - The Shenzhen set - Chest X-ray Database” having 662 images with size varying for each X-ray, approximately between 3000 x 3000 and “Montgomery County - Chest X-ray Database” with 138 images having size of 4020 x 4892 or 4892 x 4020. The two datasets have labels differentiating normal cases from images showing manifestation of tuberculosis.

3.9.2 The convolutional neural network architecture

Supervised type of learning, which is one of the machine learning algorithms, was applied. In this type of learning, the algorithm identifies features explicitly to give prediction by learning from the labelled dataset. Since the data set used was labelled, it makes supervised type of learning fit for the task.

As mentioned in the introduction, ResNet, which is one of the convolutional neural network architectures with 50 deep layers, was used.

By loading a pre-trained version of the network which is trained on more than a million images from a database, a reasonable accuracy level was accomplished. The pre-trained network can classify images into 1000 object categories, but in this case two image categories were needed: normal or indication of TB.

The network has an image input size of 224-by-224. Therefore, the previous image size of the dataset used was made to fit the network. The chest X-ray images were colour images (RGB), meaning they have 3 layers of colours. Each colour's intensity ranges from 0 - 255, 0 being very light (white) and 255 being very dark R or G or B. when we resize the image to 244 * 244, each layer will be divided to 244 columns and 244 rows.

3.9.3 Training of the model

The bit representation of colour range 255 takes a lot of space and longer processing time. So, to minimize the memory usage, both range values were divided by 255(0/255 & 255/255). This will give a new range of 0 to 1; this is called normalization. This means the image is between 0(black) and 1(white). This process is called channel reduction by rescaling.

Batch size of 32 was chosen from all the training and validation data. 32 images were taken at a time to train and validate the system.

Stochastic gradient decent (SGD) was chosen to determine the learning rate. SGD automatically fluctuates the speed of training depending on the error encountered (fast at the beginning and slow as it goes on).

As the number of training increases or the number of epoch goes down, in order to make the learning rate quadratic rather than linear, poly decay function is used.

Categorical cross entropy was chosen as loss function, which shows how far from the required 100% accuracy the training is diverging. In addition, optimizer function, which looks into the loss point and calculates the direction for converging to that 100% accuracy, was also used.

Data augmentation

Data augmentation is very important especially if the data used is small. As mentioned above, the data used was around 800 chest X-ray images.

Therefore, the need for data augmentation is unquestionable. Data augmentation is also good to reduce overfitting. Since the model will be trained with a variety of images having different positions, shifts, and flips, it would be familiar with those sorts of adjustments for the classification of new images.

In the designed model, horizontal and vertical shifts, width and height shifts and rotation were used to augment the data set.

Reduction of overfitting

A networks ability to learn could be affected by many reasons. This inability to learn effectively is called overfitting. The problem of overfitting should be avoided since it decreases a model's ability to reach its potential accuracy level. Commonly, overfitting occurs due to inappropriate learning rate, number of epochs, or data used for training or validation.

Automatic learning rate adjustment with stochastic gradient decent and the data augmentation mentioned above was applied to reduce overfitting.

Before saving the trained model, assessment was made for any sort of over or under fitting. This was done by visualizing the training and validation accuracy as well as loss values. In addition, the plot was examined if it goes down more like C curve, exponentially decreasing by reducing its loss as the training increases.

3.9.4 Results

The user interface of the deep residual learning for chest X-ray image classification was done using a pop up window. In this pop up window, there is a button asking the user to insert image or choose from saved file for the classification.

Once the image has been chosen, the system will automatically process it to predict whether the image is normal or indicates the presence of TB. During processing, if the image chosen was not appropriate or suitable, the system will display a message showing that the image is of the wrong type.

Finally, the prediction will be displayed for the user. If the user wishes to examine another chest X-ray image, the user is expected to choose another image to diagnose.

3.10 The database and user interface design of the fuzzy and rule based hybrid expert Systems

The user interface was designed using visual studio. The end user is believed to be a health professional but need not necessarily have an expert's knowledge of TB diagnosis. Having this in mind, the user interface design was made very comprehensible, easy to follow and use.

3.10.1 The database

The database was designed using SQL server. It is designed with the aim of eradicating the manual card system in TB ward. Since the medication and follow up process takes longer time, the card containing the patient's diagnosis information could get damaged during extensive use, not to mention being lost in the process.

To minimize the time spent in communicating the patient's data, examination order, examination findings and the patient's final diagnosis result among different health practitioners like the doctor, laboratory technician, radiographers, nurses and data recording office workers the database could be of great use.

On the other hand this TB patient data recording system gives easy access to patient information, to save diagnosis result and retrieve it whenever needed. Since TB medication takes a longer time, the health care giver who gives patients their medication each day needs to record the data for follow-up and progress checking. Therefore, the database helps this situation by keeping record of each patient.

The Microsoft (MS) structured query language (SQL Server)

MS SQL server is a relational database management system (RDBMS) developed by Microsoft. This database management system is used to store data so that it could be retrieved and used by other applications which are in the same computer with the database or on other computers across a network [70].

In this thesis as described above, the server is also used to store data in general. The patient information, examination results and the final diagnosis result are stored in the SQL server in a table format. Beside the patient's data, basic information of the doctors, laboratory technicians, radiographers and health care givers (nurses) is also stored. This information is used for login and user access granting.

3.10.2 The user interface design

The user interface is designed using Microsoft (MS) visual studio. This integrated development environment is used for developing "console and graphical user interface along with windows applications, web sites, web applications, and web services in both native code together with managed code" for all platforms supported by MS windows, Windows Phone and others [71].

In the thesis, it is used to build the user interface in a graphical manner and serves as an access point. By forming connection with the SQL server, it gets access to the data stored in the server. Therefore, the user interface will allow the user to process commands such as add, edit, delete as well as view data stored in the SQL server depending on the user's permission to access the data.

Beside from the above use of the visual studio, it is also connected to python in which the main program for the TB diagnosis is coded with.

The interface in which the user inserts input is built using visual studio. Once the inputs are acquired, it will be sent to the python program to be processed and the result will be sent back to the visual studio to be displayed to the user. This process will continue until the final diagnosis result is made and medication is prescribed by the python and displayed by the visual studio to the user. The overall link and communication between the python and MS visual studio is shown in figure 30.

A popup window is used to insert the patient's ID which the user want to run the diagnosis for and view the result once the python has finished processing the input. Few snapshots of the user interface designed in the current study are shown in Appendix (V).

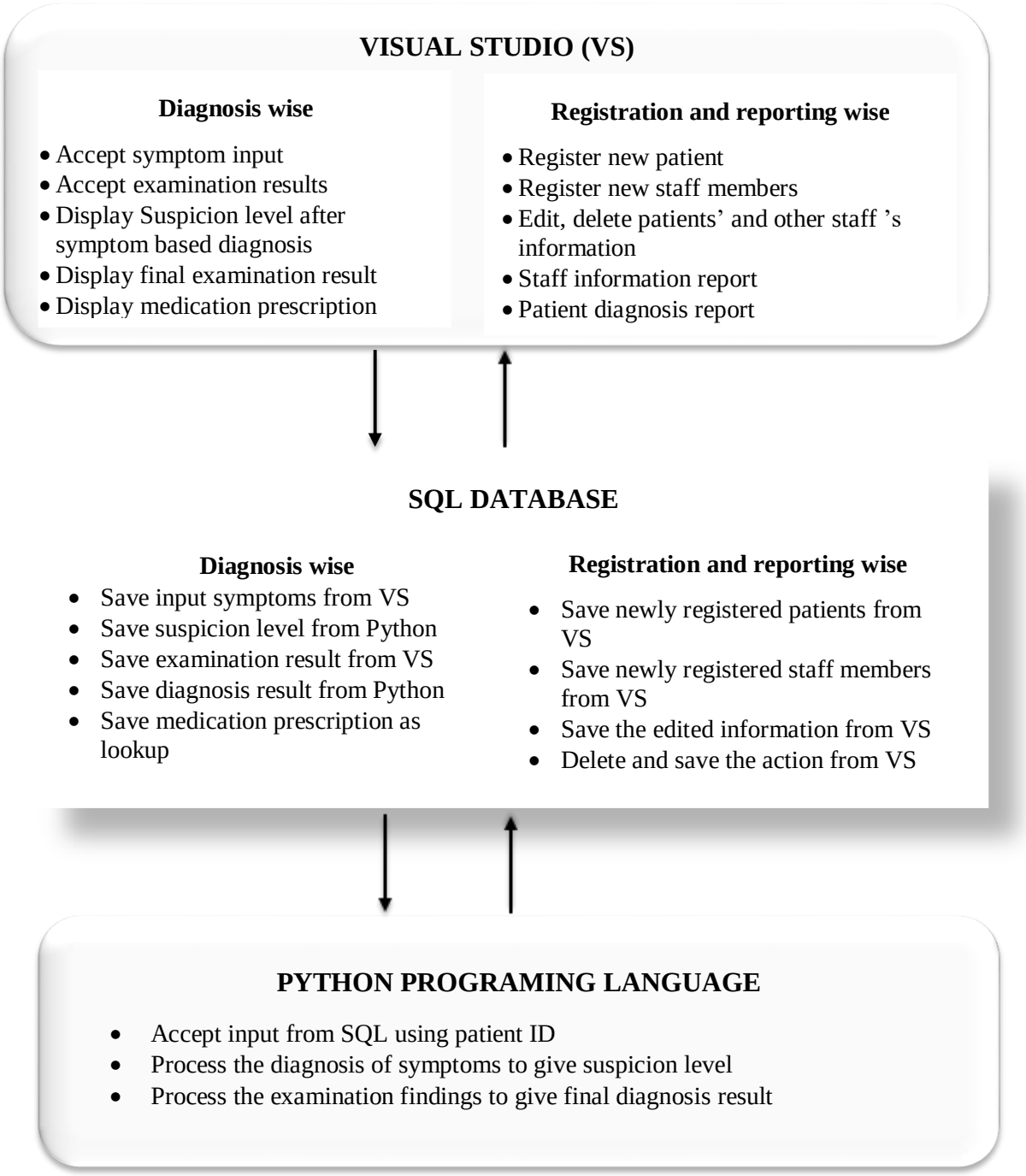


Figure 30: Link and communication between the MS visual studio, SQL server and python.

3.11 Ethical considerations

Ethical approval has been acquired from the research area and letter shown in Appendix (I), was provided to collect the necessary data. The confidentiality of the data collected was ensured. To avoid plagiarism, all works of others are cited and given appropriate credit.

3.12 Data quality assurance

Patient data was extracted from patients' diagnosis history with the help of doctors, nurses and a research assistant. From the collected patient data, 25% was used for testing the system. For the chest X-ray classification, training, validation and test data split was made automatically. The researcher made sure that the test data is introduced for prediction and evaluation only after the model has reached the required accuracy and has been saved.

3.13 Limitations of the study

Even though the doctors and internists from the research areas were very cooperative and kindly willing to help with their busy schedule, it was a very challenging task to acquire expert knowledge to design the system. If the experts had had more time to share their knowledge and data, system accuracy and generalization could have been increased. This problem is a bottle neck for development of such expert systems since the knowledge of human expert is the base of such systems. On the other hand, unavailability of organized and stored dataset of chest X-ray image was the other major difficulty faced. It would have been better if local data was included for training and testing the classification model.

CHAPTER FOUR

Data analysis

4.1 Questionnaire data analysis

The research areas as mentioned in the previous section were St. Peter's specialized hospital, Alert hospital and Bole sub-city health center. A questionnaire was prepared for nurses in the outpatient department (OPD) ward for cough related diseases. A sample of the questionnaire is presented in Appendix (II). The questionnaire respondents were all the nurses working in the TB OPD wards of the research areas; 16 nurses from St. Peter's specialized hospital, 10 nurses from Alert hospital and 5 nurses from Bole sub-city health center. Different forms were prepared to be filled out by the three domain experts in the diagnosis and treatment of TB. One internist from Alert hospital and two doctors from St. Peter's specialized hospital were kind enough to participate in the data collection in spite of their busy schedule.

To analyse the data acquired from the questionnaire, Statistical Package for the Social Sciences (SPSS) was used. SPSS is commercially distributed software suited for data management and statistical analysis [72].

In this section, sample questions from the questionnaire which were input to the designed system are presented. These data analysis samples of the questionnaire are presented in the form of number of respondents from each research areas that give response to the questions cross tabulated with the response given to the different questions. In addition, forms which were filled out by the internist and doctors, secondary data from different journals and TB guidelines that were used in the selection of input symptoms and examination modalities to the system are also discussed.

Table 16: Cross tabulation of examination ordered for patients with cough * research areas from which respondents were chosen from.

		Research areas from which respondents were chosen from (No of respondents)			
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	**Total**
Examination ordered for patients with cough	Chest X-ray	1	0	0	1
	GeneXpert, X-ray, sputum	12	8	4	24
	physical, X-ray, sputum	3	0	0	3
	Sputum, GeneXpert. FNA, chest X-ray	0	2	1	3
Total		16	10	5	31

As shown in table 16, geneXpert, chest X-ray and sputum examinations were chosen by the majority respondents of the questionnaire as diagnosis modalities for patients having cough symptom. One participant from St. Peter chose chest X-ray and three others added physical examination. Two respondents from Alert and one from Bole sub-city added fine needle aspiration (FNA) test to the three diagnosis modalities suggested by the majority.

Since the majority of nurses that participated in the questionnaire suggested chest X-ray and geneXpert as the best modalities as shown in table 16, these two examinations were taken as inputs for the designed system.

Table 17: Cross tabulation of X-ray examination for patients with cough * research areas from which respondents were chosen from.

		Research areas from which respondents were chosen from (No of respondents)			
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	**Total**
X-ray examination for patients with cough	For all Patients	9	8	3	20
	For most of the patients	7	0	2	9
	It's rarely ordered	0	2	0	2
Total		16	10	5	31

The majority respondents of the questionnaire as shown in table 17 mentioned that chest X-ray examination is ordered for all patients having cough symptoms. Seven respondents from St. Peter and 2 from Bole sub-city stated that chest X-ray examination is not ordered for all but for most of the patients having cough symptom. Only 2 nurses from Alert referred to chest X-ray as rarely ordered.

From the above assessment, we can understand that most of the patients having cough symptom were to take chest X-ray examination. In table 18, from the patients who took the examination, 50% were diagnosed to be negative for PTB. This indicates that a lot of patients who could have been spared got exposed to radiation with wrong suspicion.

Table 18: Cross tabulation of confirmed TB cases among tested with X-ray * research areas from which respondents were chosen from.

		Research areas from which respondents were chosen from (No of respondents)			
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	**Total**
Confirmed TB cases among tested with X-ray	No reply	4	2	2	8
	10-15%	1	0	0	1
	10%	1	0	0	1
	20%	1	0	0	1
	30%	1	0	1	2
	50%	8	8	2	18
Total		16	10	5	31

As shown in table 18 the majority respondents of the questionnaire mentioned that among the patients who took chest X-ray examination, 50% ended up being negative for PTB. Four respondents from St. Peter and one from Bole sub-city respectively mentioned that 10-15%, 10%, 20% and 30% of patients, who took chest X-ray examination seems to be negative for PTB.

Table 19: Cross tabulation of cough related diseases other than TB * research areas from which respondents were chosen from.

		Research areas from which respondents were chosen from (No of respondents)			Total
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	
Cough related diseases other than TB	asthma	0	2	0	2
	common cold, asthma, pneumonia	1	0	0	1
	COPD	0	2	0	2
	pneumonia	5	2	4	11
	pneumonia, asthma	0	0	1	1
	pneumonia, COPD	0	1	0	1
	pneumonia, COPD, asthma	8	3	0	11
	pneumonia, URTI	1	0	0	1
	URTI	1	0	0	1
Total		16	10	5	31

From table 19 it can be seen that the majority respondents of the questionnaire mention asthma, COPD and pneumonia as the major cough related diseases other than TB. In addition to pneumonia, upper respiratory tract infection (URTI) was mentioned by one participant from St. Peter. One participant from St. Peter mentioned URTI alone as a cough related disease other than TB, and one other participant mentioned common cold in addition to asthma and pneumonia. Therefore, pneumonia, asthma and COPD that were suggested by the majority of the respondents were used as inputs to the designed system to rule out TB.

Table 20: Cross tabulation of presence of misdiagnosed TB cases * research areas from which respondents were chosen from.

		Research areas from which respondent were chosen from (No of respondents)			Total
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	
Presence of misdiagnosed TB cases	Yes	13	8	3	24
	No	3	2	2	7
Total		16	10	5	31

As shown in table 20 the majority respondents of the questionnaire from the three research areas agreed to the existence of misdiagnosed TB cases. Only three participants from St. Peter, two from Alert and two from Bole sub-city mentioned that there are no misdiagnosed TB cases. This shows that there are misdiagnosed cases in the manual diagnosis procedure of TB, where patients will be taking medication of TB while being negative.

Table 21: Cross tabulation of medication duration for TB patients * research areas from which respondents were chosen from.

		Research areas from which respondent were chosen from (No of respondents)			
		St. Peter's Specialized Hospital(16)	Alert Hospital (10)	Bole Sub-City Health Center (5)	**Total**
Medication duration in month for TB patients	6 month for PTB	7	8	2	17
	6 month for PTB, 9-12 month for bone, mening, CNS TB	2	2	1	5
	6 months for PTB & dependant for EPTB	4	0	1	5
	6 months for PTB and 9 months for GIT. CNS, Mening	3	0	1	4
Total		16	10	5	31

All respondents of the questionnaire as shown in table 21 said that six months of anti-TB medication is prescribed for treatment of PTB. For EPTB, two respondents from Alert, two from St. Peter's and one from Bole sub-city mentioned 9-12 month of anti-TB medication for bone, meninges and CNS TB. Four participants from St. Peter and one from Bole sub-city implied that the medication for EPTB is dependent on the area affected. The rest three from St. Peter and one from Bole sub-city mentioned that 9 months of anti-TB medication is needed for TB of GIT, CNS and Meninges.

Therefore, as an input to the designed decision support system, the medication duration suggested by the majority participants of the questionnaire which was, 6 month for PTB and 9 month for CNS, GIT, bone and Meninges were taken.

Table 22: Cross tabulation of the need for diagnosis supportive system * research areas from which respondents were chosen from.

		Research areas from which respondents were chosen from (No of respondents)			
		St. Peter's Specialized Hospital(16)	Alert Hospital(10)	Bole Sub-City Health Center(5)	**Total**
The need for diagnosis supportive system	Yes	16	10	5	31
Total		16	10	5	31

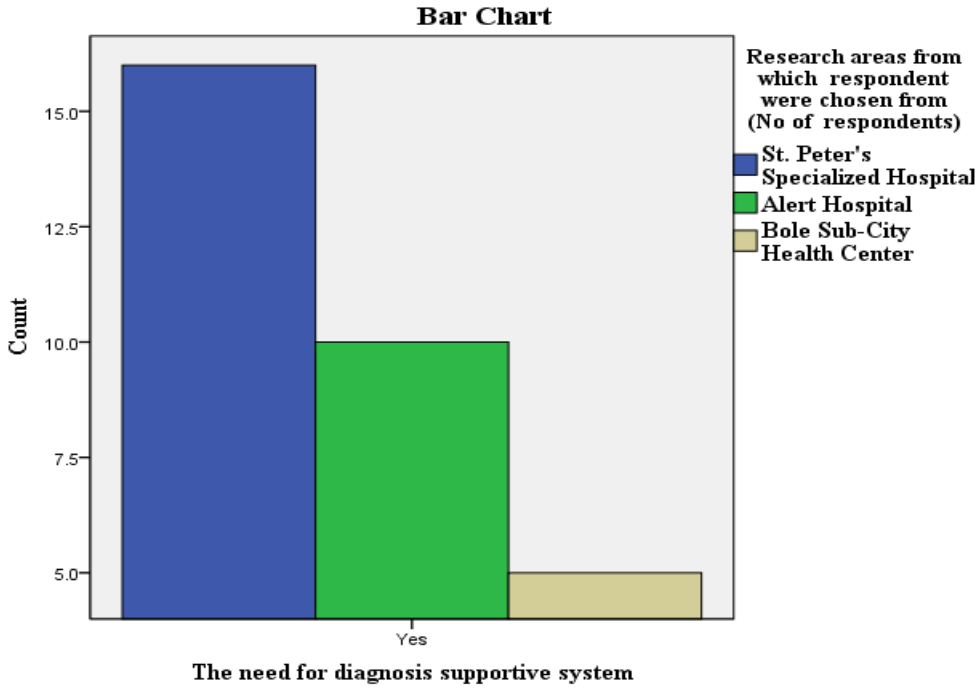


Figure 31: Questionnaire participants' reaction to the need for diagnosis supportive system.

As shown in table 22 and figure 31, all the respondents from the three research areas agreed to the necessity of a decision supportive system for the diagnosis of TB.

4.2 Input data analysis for the designed system

The Fuzzy portion of the designed decision support system uses symptoms of the selected diseases as an input. The second phase of the decision support system, which is rule based, uses examination findings as an input. The symptoms and examination findings for each disease were chosen with the help of 3 doctors.

From the questionnaire, three cough related diseases that mimic PTB which were mentioned by the majority of the respondents were taken. To double check and confirm those three diseases, the doctors' opinions were also included. On the other hand, TB can affect any part of the human body. Therefore, EPTB sites are very large in number and incorporating all those types of EPTB in the designed system is not feasible. As a result, the most prevailing ones in the diagnosis experience of the participating doctors were chosen. In the next part of the data analysis, sample of the selection process of the EPTB diseases, symptoms and examinations are presented.

Table 23: Doctors' suggestion on cough related diseases that mimic TB and EPTB diseases that occur frequently.

Health Professionals	Cough related disease that mimic TB	EPTB that occur frequently based on experience in the diagnosis of TB	Conclusion
From Int. in Alert H.	Pneumonia, COPD, Asthma, Heart failure	Bone and joint, Spine, GIT, UTI, Lymph-node, Meninges	**Cough related disease that mimic TB:** Pneumonia, Asthma and COPD
From Dr.1 in St. Peter S. H.	Common cold, Asthma, Pneumonia, Bronchitis, Lung fibrosis	Pericardial, Spine, GIT , Lymph-node, Meninges	**Frequently occurring EPTB diseases:** Osteo-articular (Spine, bone and joint), GIT, Lymph-node and Meninges
From Dr.2 in St. Peter S. H.	COPD, Pneumonia	Pleural, Bone and joint, Lymph-node, CNS, Abdominal	

As we can see from the conclusion column of table 23, almost all the three doctors confirmed the cough related diseases mentioned by nurses who participated in the questionnaire. Therefore, pneumonia, asthma and Chronic obstructive pulmonary disease (COPD) were selected to rule out TB in the designed system. The major EPTB diseases encountered by the three doctors in their experience were: osteo-articular TB (spine, bone and joint), TB of GIT, TB of lymph-node and TB of meninges. These four EPTB diseases were selected for the system.

Once the choices of the diseases were completed, the next step was finding out symptoms as accurately as possible which most likely suggest presence of each selected disease.

Table 24: Symptoms of PTB that were found from 10 different literatures and the commonly stated symptoms as a final conclusion.

No	From [55]	From [58]	From [51]	From [73]	From [53]	From [52]	From [57]	From [74]	From [75]	From [76]	Final comparison (final count)
1	Chest pain	Cough > 3 weeks	Chronic cough	Cough > 3 weeks	Cough	Chest pain	Cough	Loss of appetite	Complaint of cough	Ache on chest	Cough (11)
2	Cough duration	Coughing up blood	Weight loss	Weight loss	Body Temp	Weight loss	Blood with cough	Confusion	Chest pain	Weakness	Chest pain, (7)
3	Night sweats	Chest pain	Intermittent fever	Fever	Fever	Cough	Chest pain	Cough	Weight loss	Complaint of cough	Night sweats (9)
4	Loss of appetite	Unintentional weight loss.	Night sweats	Drenching night sweats	Sputum discoloration	Night sweats	Fatigue	Fever	Night sweats	Dyspnoea on exertion	Loss of appetite (6)
5	Coughing up blood	Fever.	Coughing blood.	Loss of appetite	Nose sputum	Fever	Fever	Chest pain	Fever	Habit of cigarette	Blood with cough (4)
6	Fatigue	Night sweats		Anaemia	Afternoon chills	Shortness of breath	Lack of appetite	Weight loss	Shortness of breath	Rattle in chest	Fatigue (3)
7		Chills (shivering)		Sputum	Night sweats		Weight loss	Night sweat		Pressure on chest	Unintentional weight loss. (10)
8		Loss of appetite.		Mantoux	Weight loss		Night sweating	Fatigue		Sputum	Intermittent fever (9)
9					Loss of appetite			Meningitis		Sound on R. tract	Chills (shivering)

Table 25: Final conclusion from the literatures and the suggestion from the three doctors.

No	Final Comparison from literatures on PTB (final count)	From Int. in Alert H.	From Dr.1 in St. Peter S. H.	From Dr. 2 in St. Peter S. H.	Final comparison (final count)
1	**Cough(11)**	**Breathing rate**	**P. Cough**	**Productive cough**	**Cough (4)**
2	**Chest pain (7)**	**Weight loss**	**Breathing rate**	**Intermittent fever and Chest pain**	**Chest pain (4)**
3	Night sweats (9)	**Shortness of breath**	Mild headache	Night sweet	**Breathing rate (3)**
4	Loss of appetite (6)	Night sweats	Loss of appetite	**Weight loss**	**Unintentional weight loss (4)**
5	Blood with cough (4)	**Cough**	**Weight loss**	**Shortness of breath**	**Shortness of breath (3)**
6	Fatigue (3)	**Chest pain**	**Shortness of breath**	**Breathing rate**	
7	**Unintentional weight loss (10)**		Fatigue		
8	Intermittent fever Duration (0-30 days) (9)		**Chest pain**		
9	Chills (shivering)				

PTB symptoms from ten different literatures were compared and the most frequently mentioned were selected as shown in table 24. In table 25, those selected PTB symptoms were compared with the suggestion of the three doctors. Sample of doctor's suggestion is presented in Appendix (III). High priority was given to the suggestion of the doctors since those suggestions were based on their experience in their day to day diagnosis activities. Finally, PTB symptoms with high probability of indicating the presence of the disease were selected. The same procedure was followed for selecting symptoms of the chosen EPTB diseases.

Table 26: Examinations which are used to diagnose PTB from 7 different literatures as well as TB guidelines and the commonly stated examinations as a final conclusion.

No	From [77]	From [78]	From [79]	From [80]	From [81]	From [82]	From [23]	Final comparison (final count)
1	**Mantoux tuberculin skin test**	**Smear microscopy**	Chest X-rays	**The tuberculin skin test (tst)**	Chest X-ray	Tb culture test	Chest X-ray	**Tuberculin skin test (5)**
2	**Interferon-gamma release assays**	**Culture**	**Sputum smear microscopy**	**Interferon-γ release assays (igras)**	**Staining for acid fast bacilli (afb)**	**Tb skin test**	Chest CT	**Interferon gamma release assay (5)**
3	Chest X-ray/ sometimes CT scan	**Nucleic acid amplification**	**Culture**	**Smear microscopy**	**Solid media culture (Mycobacterial culture)**	**Tb interferon gamma release assays**	**AFB smear microscopy**	Chest X-ray (5)
4	Specimen collection, processing, and review	DNA hybridization and mutation detection	**Genexpert**	**Culture**	**Interferon gamma release assays**	**Sputum smear microscopy**	**Culture**	**Nucleic acid amplification testing (3)**
5	**Afb smear classification and results**	**HIV-test**	**Tuberculin skin test**	**Cultures/sputum using molecular assays and immunoassays**	**Fluorescent afb stains for tuberculosis**	Fluorescent microscopy	**Nucleic acid amplification testing**	**Mycobacterial culture (7)**
6	**nucleic acid amplification**		**Interferon gamma release assay**	**HIV-test**	**Tuberculin skin test (tst)**	Chest X-ray	**HIV-test**	**Staining for acid fast bacilli (7)**
7	**Culture**				**Liquid media culture**	**HIV-test**	**Xpert mtb/rif (cepheid)**	**Genexpert test (3)**
8	**HIV-test**				**HIV-test**	**Genexpert test**		**HIV-test**

Table 27: Final conclusion from table 26 and the suggested examinations for PTB diagnosis from the three doctors.

No	Final comparison (final count)	From Int. in Alert H.	From St. Peter Hosp. Dr. 1	From St. Peter Hosp. Dr. 2	Final conclusion (final count)
1	Mantoux tuberculin skin test (tst) (5)	AFB	**Genexpert**	CBC	**Chest X-ray (4)**
2	Interferon gamma release assay (igra) (5)	**Chest X-ray**	**CXR**	**ESR**	**Genexpert (4)**
3	Nucleic acid amplification testing (4)	**Genexpert**	**CBC/ESR**	**Genexpert**	**ESR (3)**
4	**Chest X-ray (5)**	**ESR**	PHICF	**CXR**	**HIV test (2)**
5	Mycobacterial culture (7)	**HIV- test**			
6	Staining for acid fast bacilli (afb) (7)				
7	**Genexpert test (4)**				
8	Line probe assay (3)				
9	**HIV test (7)**				
10	Antibody and antigen detection				
11	Drug-susceptibility testing				
12	Polymerase chain reaction				

In table 26, PTB examination modalities from seven different literatures and guidelines were compared and the most frequently mentioned were selected. Those selected examinations were compared with the suggestions from the three doctors as shown in table 27. Sample of doctor's suggestion is presented in Appendix (III). By giving priority to the doctors' suggestion, PTB examinations with high chances of indicating PTB and which are highly available were selected. The same procedure was followed in selecting examinations for the chosen EPTB diseases.

Table 28: Different examinations for the chosen EPTB diseases that were taken from different literatures.

1. TB OF MENINGITS [83] - [88]	2. TB OF GIT [89] - [94]	3. TB OF LYMPHADENITIS [95] - [100]	4. OSTEO-ARTICULAR TB [101] - [107]
CSF WBC count (elevated) (3)	Plain abdominal series (3)	Smears(FNA cytology) (3)	Tuberculin skin test (6)
CSF protein (elevated) (5)	Chest X-ray (2)	PCR (4)	IGRAs (3)
CSF glucose (4)	Abdominal ultrasound (6)	Lymph node biopsy (4)	CT (3)
leukocytosis (WBC > 11.0 × 109/Liter) (3)	CT of the abdomen (5)	Microscopy and culture of the pus (3)	MRI (4)
Chest X-ray(mostly non-specific changes) (2)	Colonoscopic findings (4)	Tuberculin skin test (sensitivity is very less) (3)	PCR on obtained joint tissue biopsies (3)
MTB culture(positive) (4)	Laparoscopic findings (3)	Ultrasound of the neck (2)	synovial fluid aspiration for bacteriological examination(3)
CT (5)	Ascetic Fluid Culture (4)	Histological examination (2)	Biopsy (3)
MRI (5)	CT combined with guided needle aspiration biopsy (3)	Chest radiograph of the neck	Bacteriology (3)
PCR and CSF (3)	Barium contrast Studies (3)	Ct of the neck	Histology (2)
nucleic acid amplification (2)	Endoscopy (3)	MRI of the neck	Sputum culture (2)
Tuberculin skin test (2)	Histopathology (2)	Chest X-ray	Fine needle aspiration biopsy
T-cell-based (IGRAs) (2)	Culture	AFB smear	Chest radiographs
Sputum (2)	Nucleic acid amplification		Smear for acid-fast bacilli
Lumbar puncture	Genexpert Assay		Nucleic acid amplification
	Tb PCR		Autopsy
			Serological tests
			Differential white cell count

From different guidelines and literatures, different examinations were collected and the form shown in table 28 was prepared. The prepared form was reviewed by doctors and laboratory technicians and those examinations which had to be conducted and which were available were chosen (the green shaded ones).

Table 29: Medication prescription from five different TB guidelines.

1. From [108]			**2. From [109]**					**3. From [83]**			
Drug Name	**Adult Dosages**		**Month of treatment**	**Drug**	**Weight in Kg**			**Drug**	**Daily**		**3 times/week**
	Daily	Thrice-Weekly			30-39	40-55	>55				
Isoniazid (H)	5 mg/kg to 300 mg	15 mg/kg to 900 mg	1-2 Intensive phase	(RHZE) R-150 mg, H-75 mg Z-400 mg, E-275 mg Combine tablets	2	3	4	**H**	5 mg/kg (300 mg)		15 mg/kg (900 mg)
								R	10 mg/kg (600 mg)		10 mg/kg (600 mg)
								Z	weight		
Rifampicin (R)	10 mg/kg to maximum 600 mg in practice 450 mg if <50 kg, 600 mg if ≥50 kg)	600 mg	3-6 continuation phase	(RH) R-150 mg H-75 mg Combine tablets	2	3	4		40– 55 kg	56– 75 kg	76– 90 kg
								Daily	18.2– 25 mg/kg (1000 mg)	20– 26.8 mg/kg (1500mg)	22.2– 26.3 mg/kg (2000 mg)
Ethambutol (E)	15 mg/kg	30 mg/kg	H = Isoniazid,R = rifampicin, Z = pyrazinamide, E = ethambutol					3 times/ week	27.3– 37.5 mg/kg (1500 mg)	33.3– 44.6 (2500 mg)	33.3– 39.5 mg/kg (3000 mg)

Pyrazinamide (Z)	30–40 mg/kg to max 2 g (in practice 1.5 g if <50 kg, 2 g if ≥50 kg)	2 g if <50 kg, 2.5g if ≥50 kg	For new TB cases the adult dosage should be based on their weight and contents of the tablets
Pyridoxine (B6)	25mg	50mg	
The standard treatment regimen is six months of isoniazid and rifampicin, Supplemented in the first two months by pyrazinamide, and by ethambutol.			

	weight		
E	40– 55 kg	56– 75 kg	76– 90 kg
Daily	14.5– 20 mg/kg (800 mg)	16– 21.4 mg/kg (1200 mg)	17.8– 21.1 mg/kg (1600 mg)
3 times/ week	21.8– 30 mg/kg (1200 mg)	26.7– 35.7 mg/kg (2000 mg)	26.7– 31.6 mg/kg (2400 mg)
INH= isoniazid RIF= rifampin RBT= rifabutin RPT= rifapentine PZA= pyrazinamide EMB= ethambutol			
For purposes of this document, adult dosing begins at age 15 years. Children weighing more than 40 kg should be dosed as adults. Adjust doses as the patient's weight changes.			

Table 30: Medication prescription from five different TB guidelines continued from table 29.

4. From [110]					**5. From [111]**					
Drug	**daily**		**3 times per week**		**Drug**	**Daily**		**3 times per week**		
	dose and range (mg/kg body weight)	max (mg)	dose and range (mg/kg body weight)	daily max (mg)		Dose and range (mg/kg body weight)	Max (mg)	Dose and range (mg/kg body weight)	Daily maximum (mg)	
Isoniazid (H)	5 (4–6)	300	10 (8–12)	900	H	5 (4-6)	300	10 (8-12)	900	
Rifampicin (R)	10 (8–12)	600	10 (8–12)	600	R	10 (8-12)	600	10 (8-12)	600	
Pyrazinamide (Z)	25 (20–30)	-	35 (30–40)	-	Z	25 (20-30)	2000	35 (30-40)	2000	
Ethambutol (E)	15 (15–20)	-	30 (25–35)	-	E	15 (15-25)	1200	30 (20-35)	1200	
Streptomycin (S)	15 (12–18)		15 (12–18)	1000	S	15 (12-18)	1000	15 (12-18)	1000	
Intensive phase treatment		Continuation phase			TB case classification		Dosing frequency		TB treatment regimen	
2 months of HRZE		4 months of HR							Initial phase	Continuation phase
“WHO no longer recommends omission of ethambutol during the intensive phase of treatment for patients with non-cavitary, smear-negative PTB or EPTB who are known to be HiV-negative. In tuberculous meningitis, ethambutol should be replaced by streptomycin. H = isoniazid, r = rifampicin, Z = pyrazinamide, e = ethambutol, S = streptomycin”					New patients with drug-susceptible TB both HIV-positive and HIV-negative patients, and those with EPTB (except TB of meninges , CNS, joint and bone).		PREFERRED treatment regimen Daily for initial and continuation phases		2 HRZE	4HR

In order to find the medication for PTB and the four EPTB diseases, five different TB guidelines were reviewed as shown in table 29 and 30.

Table 31: General medication prescription for PTB and the chosen 4 EPTB diseases.

Active Pulmonary TB	1. TB OF MENINGITS	2. TB OF GIT	3. TB OF LYMPHADENITIS	4. OSTEO-ARTICULAR TB
6 month regimen containing isoniazid, rifampicin and pyrazinamide for 2 months followed by isoniazid, riframpicin for 4 months given on daily basis or on intermittent basis	Initial two month course of intensive therapy using the four first line therapies (isoniazid, rifampicin, pyrazinamide, and ethambutol) followed by a prolonged course lasting 7 - 10 months, of 2 drugs (isoniazid and rifampicin) (3)	Anti-tubercular therapy for at least 6 months including initial 2 months of rifampicin, isoniazid, pyrazinamide and ethambutol followed by a prolonged course lasting 4 months, of 2 drugs (isoniazid and rifampicin)	6 month regimen containing isoniazid, rifampicin and pyrazinamide for 2 months followed by isoniazid, riframpicin for 4 months given on daily basis or on intermittent basis	6- to 9-month regimens (2 months of isoniazid and rifampicin, pyrazinamide, and ethambutol followed by 4-7 months of inh and rif) are recommended as initial therapy unless the organisms are known to be or strongly suspected of being resistant to the first-line drugs
2(RHZE), 4(RH)			2(RHZE), 4(RH)	

As table 31 shows, a form was prepared which contains general medication prescription and duration of intake from the five guidelines shown in table 29 and 30. This form was given to the three doctors to confirm and assess if any change was needed. As shown in table 31, three medication prescriptions were agreed upon and the two needed some change. Therefore, by making the suggested changes and discussing the dosage, medication prescriptions for the designed system were taken.

CHAPTER FIVE

Results and Discussion

In this chapter, preparations of symptoms and examination findings from patients' diagnosis history which are input to the system are shown. Then the results obtained while applying the designed expert system on the test data is presented. A summary of the predicted result in comparison to the actual result given by the doctors is also shown. Performance evaluation of the fuzzy and rule based hybrid expert system as well as the chest X-ray classification is presented by using performance evaluation metrics such as accuracy, sensitivity, specificity and processing time. Finally, the results obtained in comparison to other works in literatures are discussed.

5.1 Result

5.1.1 Test data preparation

From the overall data collected, 25% was taken for performance evaluation which comprises of 20 patients. The choice of the patients' data was made purposively as it would help to assess the system's functionality. Patients with the age of 15 to 65 were chosen; five patients diagnosed for PTB, ten patients for EPTB and the rest five patients with asthma, pneumonia and COPD. The patients' data was organized in a way that the system requires.

Linguistic variables (mild, moderate, severe) which are briefly explained in the material and methodology section are used to assign symptoms severity levels.

For example, for a patient with a cough symptom:

- If the cough is dry, then mild value with a score of 1 up to 4 will be given
- If the cough is with sputum, then moderate value with score of 4 up to 7 will be given and
- If the cough is with sputum containing blood, then severe value with score from 7 up to 10 will be given.

The organization of the severity level of symptoms experienced by the chosen patient with PTB, the three cough related diseases (asthma, COPD and pneumonia) and the four types of EPTB diseases which are taken for testing system performance are shown in table 32, 33 and 34.

Table 32: Symptom severity level of the five PTB patients which were taken for testing the system.

	Severity of patient's symptom (Range of severity)						
PTB Patient ID	**Cough**	**Shortness of breath**	**Respiratory rate**	**Fever**	**Chest pain**	**Unintentional weight loss**	**Age**
001	Mild (3)	Sever (8)	Moderate (30)	Mild (2)	Moderate (5)	Mild (2)	Moderate (6)
002	Moderate (4)	Mild (1)	Mild (20)		Mild (2)	Mild (1)	Severe (8)
003	Mild (2)	Mild (2)	Severe (32)		Severe (9)	Mild (1)	Mild (3)
004	Mild (1)	Mild (1)	Moderate (25)		Mild (3)	Mild (1)	Moderate (7)
005	Moderate (5)	Mild (2)	Mild (18)		Mild (2)	Moderate (7)	Mild (3)

Table 33: Symptom severity level of the asthma, pneumonia and COPD patients which were taken for testing the system.

	Severity of patient's symptom (Range of severity)						
Asthma Patient ID	**Wheezing**	**Cough at night or with environmental stimuli**		**Fever**	**Shortness of breath at night or with environmental stimuli**		**Age**
006	Moderate (4)	Severe (8)		Mild (1)	Moderate (7)		Mild ()
Pneumonia Patient ID	**Cough**	**Confusion**	**Respiratory rate**	**Fever**	**Unintentional weight loss**	**BP**	**Age**
007	Moderate (7)	Severe (7)	Severe (34)			Mild (2)	Moderate (4)
008	Severe (7)	Moderate (4)	Mild (23)		Severe (9)	Moderate (4)	Moderate (4)
COPD Patient ID	**Cough**	**Wheezing**	**Edema**	**Fever**	**Shortness of breath**		**Age**
009	Mild (4)	Mild (3)	Severe (9)	Severe (8)	Severe (8)		Mild (3)
010	Severe (7)	Mild (3)	Moderate (5)	Moderate (4)	Severe (8)		Mild (3)

Table 34: Symptom severity level of the ten EPTB patients which were taken for testing the system.

	Severity of patient's symptom (Range of severity)					
TB of GIT Patient ID	**Abdominal pain**	**Change in bowl habit**	**Loss of appetite**	**Fever**	**Abdominal Swelling**	**Nausea**
001	Sever (8)	Moderate (5)	Mild (3)	Mild (1)	Moderate (5)	Moderate (5)
002	Moderate (5)	Mild (3)	Moderate (5)		Severe (8)	Mild (3)
003	Mild (3)	Moderate (5)	Moderate (5)	Mild (1)	Moderate (5)	Moderate (5)
TB of Meninges Patient ID	**Stiff neck**	**Meningeal Sign**	**Altered mental status**	**Weakness**	**Headache or Fever**	
004	Severe (8)	Moderate (5)	Mild (3)	Moderate (5)	Moderate (5)	
005	Mild (2)	Mild (1)	Mild (2)	Moderate (5)	Mild (3)	
TB of Osteo-articular Patient ID	**Headache or Fever**	**Swollen bone or joint**	**Restriction of movement**	**Pain**	**Draining Sinus**	
006	Severe (8)	Moderate (5)	Severe (8)	Moderate (5)		
007	Moderate (5)	Severe (8)	Moderate (5)	Moderate (5)	Severe (8)	
008	Moderate (5)	Mild (2)	Moderate (4)	Moderate (4)	Mild (1)	
TB of Lymph-node Patient ID	**Mass along the nick**	**Unintentional weight loss**	**Fever**			
009	Severe (8)	Mild (3)	Moderate (5)			
010	Moderate (5)	Moderate (5)	Mild (3)			

5.1.2 Performance evaluation

I. Performance evaluation of the fuzzy and rule based hybrid expert system

a. Evaluation of system's performance in predicting disease suspicion level

After the symptoms' severity level and range is assigned, it is inserted into the system to find level of suspicion for the four cough related diseases namely: asthma, pneumonia, COPD and PTB and for the four EPTB diseases as well. The user's guide on how to choose severity level of patient's symptom is clearly shown in Appendix (V).

The disease suspicion level prediction of the system is compared with the doctor's suspicion in order to run examination. This comparison shows the generalization capability of the system by using patient's symptoms. Comparison between system prediction and the doctors is shown in table 35.

Table 35: Comparison of system's prediction with the doctors for cough related diseases.

Patient ID	System Suspicion (range of suspicion from 1 to 10)	Doctor Suspicion
001	**PTB (6.46),** COPD (5.82), Pneumonia (4.58), Asthma (1.72)	PTB
002	**Pneumonia (6.13),** PTB (4.65), COPD (1.75), Asthma (1.72)	PTB
003	**PTB (8.14)**, Pneumonia (3.54), COPD (3.37), Asthma (1.72)	PTB
004	Pneumonia (4.77), PTB (4.2), COPD (1.86), Asthma (1.72)	PTB
005	**PTB (5.0)**, Pneumonia (4.2), COPD (3.37), Asthma (1.72)	PTB
006	**Asthma (6.46)**, PTB (1.72), Pneumonia (1.72), COPD (1.75)	Asthma
007	**PTB (5.8), Pneumonia (5.8),** COPD (4.71), Asthma (1.72)	Pneumonia
008	**PTB (5.8)**, Pneumonia (5.42), COPD (4.71), Asthma (1.72)	Pneumonia
009	**COPD (8.06)**, PTB (6.63), Pneumonia (4.2), Asthma (1.92)	COPD
010	**PTB (6.46)**, **COPD (6.46),** Pneumonia (5.0), Asthma (1.94)	COPD

Systems' prediction of the suspicion level of the four diseases was 70% similar with the doctors as shown in table 35.

Unlike the doctors' prediction, the system gives the probability of a patient having the four cough related diseases (PTB, pneumonia, asthma and COPD) with values expressed in ranges between one and ten. Suspicion values greater than or equal to five are qualified for examination.

This is helpful for the user to have all the possibilities to consider. This prevents user from ordering multiple examinations to rule out each of the suspected diseases. This in turn saves patients from unnecessary tests and exposure to radiation based on wrong suspicion and also saves their time and money.

Table 36: Comparison of system's prediction with the doctors for the four EPTB diseases.

Patient ID	System Suspicion (range of suspicion from 1 to 10)	Doctor Suspicion
001	**GIT (6.46),** Osteo (1.72), Mening (1.72), Lymph. (1.72)	GIT
002	**GIT (6.46),** Osteo (1.72), Mening (1.72), Lymph. (1.72)	Obstruction of intestinal tract
003	**GIT (5.0),** Osteo (1.72), Mening (1.72), Lymph. (1.72)	GIT
004	**Mening (6.46),** GIT (1.72), Osteo (1.72), Lymph. (1.72)	Mening
005	Mening (4.2), GIT (1.72), Osteo (1.94), Lymph. (1.72)	Mening
006	**Osteo (6.63),** Mening (6.11), GIT (1.72), Lymph. (1.72)	Osteo
007	**Osteo (6.63),** Mening (1.72), GIT (1.72), Lymph. (1.72)	Osteo
008	Osteo (4.65), Mening (1.72), GIT (1.72), Lymph. (1.72)	Osteo
009	**Lymph (6.63),** Osteo (1.72), Mening (1.72), GIT (1.72)	Lymph
010	**Lymph (5.0),** Osteo (1.72), Mening (1.72), GIT (1.72)	Lymph

Similarly for EPTB diseases, the system recommends running examination for disease suspicion level greater than or equal to five. The disease which has the highest percentage of suspicion among the four EPTB diseases was compared with suspicion of the doctors for the 10 patients.

As shown in table 35, the highest suspicion values given by the system for patient ID 002 was different from the doctors'. For patients with ID number 005 and 008, system suspicion was lower than five; therefore, the system does not recommend to conduct any examination for the four EPTB diseases, but the doctors suspected TB of meninges and osteo-articular TB respectively and ordered further examination for the two patients. For such cases, even if the doctor's suspicion matches with the suspicion of the system, these suspicions were not considered as similar because the doctor ordered further examination based on his/her suspicion while the system does not recommend examination due to the level of suspicion obtained. By considering these cases, system suspicion is 70% similar with that of the doctors as shown in table 36.

b. Evaluation of system's ability to predict final diagnosis result

After finding the highly suspected disease in both cough related and EPTB diseases, examination finding analysis was performed. Examination analysis includes the chest X-ray image classification performed by the system as one examination finding for PTB. The final diagnosis result prediction of the system for both PTB and EPTB was then compared with the final diagnosis decision made by the doctors as shown in table 37 and 38.

Table 37: PTB final diagnosis result comparison for the 10 patients which were taken for testing the system.

P. ID	**Disease for which examination was ordered for**	**System final diagnosis result**	**Doctor final diagnosis result**	**Duration of Anti TB medication prescription by the system**	**Duration of Anti TB medication prescription by Doctors**
001	PTB	+ve for PTB	+ ve for PTB	6 months	6 months
002	PTB	-ve for PTB	-ve for PTB	-	-
003	PTB	+ve for PTB	+ ve for PTB	6 months	6 months
004	PTB	-ve for PTB	-ve for PTB	-	-
005	PTB	+ve for PTB	+ ve for PTB	6 months	6 months
006	Asthma	Suggested to be examined 1st level	+ ve Asthma	-	-
007	Pneumonia	Suggested to be examine 1st level with PTB	- ve Pneumonia	-	-
008	Pneumonia	Suggested to be examine 2nd level	+ ve Pneumonia	-	-
009	COPD	Suggested to be examine 1st level	+ ve COPD	-	-
010	COPD	Suggested to be examine 1st level with PTB	+ ve COPD	-	-

Final diagnosis prediction of the system for all 5 patients suspected of having PTB were the same with that of the doctors and they were correctly diagnosed. From the rest 5 diseases for which the system does not include examination analysis, 3 of them were correctly predicted with the highest suspicion. The remaining 2 were suspected wrongly by the system from which one of them was also wrongly suspected by the doctor.

Table 38: EPTB final diagnosis result comparison for the 10 patients which were taken for testing the system.

P. ID	**Disease for which examination was ordered for**	**System final diagnosis result**	**Doctor final diagnosis result**	**Duration of Anti TB medication prescription by the system**	**Duration of Anti TB medication prescription by Doctors**
001	TB of GIT	+ve for TB of GIT	+ve for TB of GIT	6 months	6 months
002	TB of GIT	+ ve for TB of GIT	+ ve for TB of GIT	6 months	6 months
003	TB of GIT	+ ve for TB of GIT	+ ve for TB of GIT	6 months	6 months
004	TB of Meninges	+ ve for TB of Meninges	+ ve for Meninges	9 months	9 months
005	TB of Meninges	- ve for TB of Meninges	- ve for TB of Meninges	-	-
006	TB of Osteo-A.	+ve for TB of Osteo-A.	+ve for TB of Osteo-A.	9 months	9 months
007	TB of Osteo-A.	+ ve for TB of Osteo- A.	+ ve for TB of Osteo-A.	9 months	9 months
008	TB of Osteo-A.	- ve for TB of Osteo- A.	- ve for TB of Osteo- A.	-	-
009	TB of Lymph-N.	+ ve for TB of Lymph-N.	+ ve for TB of Lymph-N.	6 months	6 months
010	TB of Lymph-N.	+ve for TB of Lymph-N.	+ve for TB of Lymph-N.	6 months	6 months

Final diagnosis prediction of the system for all the 10 patients suspected of having different forms of EPTB were confirmed by the examinations and the system's suspicion was found out to be correct for all the patients. The three cases (Patient ID 002, 005 and 008 in table 38), which were suspected by the doctors were found to be wrong suspicions since they turned out to be negative.

c. Overall system performance evaluation

After analysis of the system's prediction in relation to the true diagnosis result, the designed system accuracy was evaluated by the fraction of predictions the system got right [112].
Since examinations will not be analysed by the system for asthma, COPD and pneumonia, when calculating the system accuracy, if the system does not have a higher suspicion percentage for the disease which is suspected by the doctors, this value is considered as false positive like the case of patient ID 007 in table 37. At the same time, if the doctors do not suspect the presence of one of the three diseases but the system suspicion percentage is the highest for the respective disease, this case was taken as false negative like the case of patient ID 008 in table 37.

Table 39: The fuzzy and rule based hybrid expert system prediction.

	System Predictions					
	TP	**TN**	**FP**	**FN**	**Execution time per case (after system start running)**	**No. of Cases**
✓ ***PTB detection***	3	2			3 sec.	5
✓ ***The other cough related diseases suspicion***	3		1	1	3 sec.	5
✓ ***EPTB detection***	7	3	0	0	2 sec.	10
✓ ***System over all Prediction***	13	5	1	1		20

From the total of 80 patients' diagnosis data, 25% which are 20 patients were taken for evaluating the system's performance. Once the true positive (TP), true negative (TN), false positive (FP) and false negative (FN) prediction of the system for the 20 (10 EPTB, 5 PTB and the rest 5 pneumonia, asthma and COPD) patient cases were found as shown in table 39, system accuracy (Acc) was calculated by using the following equation.

$$Acc = \frac{TP + TN}{TP + TN + FP + FN}$$

Table 40: Accuracy of the designed system.

PTB detection accuracy of the system = 0.867		**EPTB detection accuracy of the system = 1.0**
	Average system accuracy 0.933	

In order to effectively examine the system's performance, prediction of the system was evaluated independently for the diagnosis of PTB and EPTB. As shown in table 40, the system achieved a very good accuracy level for both predictions. Especially for EPTB diagnosis from which misdiagnosis cases are very common, system performance was very encouraging. The designed fuzzy and rule based hybrid expert system diagnoses a patient for TB by first ruling out PTB from the major cough related diseases and then examining the patient for the major EPTB diseases. This does not mean that the PTB and EPTB diagnosis are separate but a single diagnosis procedure a patient passes through. Thus, average system accuracy was calculated to find the final system performance.

After performing the calculation, the system was found to have a remarkable diagnosis accuracy of 93% and execution time of less than a minute as shown in table 39 and 40. This was very encouraging and promising. The system would be helpful to assist medical practitioners in the diagnosis of TB. The good quality of expert systems can be witnessed here, providing accurate results in a very short execution time. The results obtained on real patients' data confirms that the fuzzy logic expert system can represent an expert's thinking in handling complex trade-offs.

II. System's chest X-ray image classification performance evaluation

The performance of the chest X-ray image classification model was evaluated by using 10% of the data set which are 80 pre-labeled images. The evaluation was performed over different metrics. These metrics include accuracy, sensitivity (recall), specificity and precision. Confusion matrix table was used to obtain the classifier accuracy. Python commands, classification report and confusion matrix were used to obtain the performance measuring parameters.

The model was trained by using 80% training and 10% validation data. The classification report of the validation data, which has 72 images, indicates that the model got 0.94% precision for predicting images that are indicative of PTB and 0.87% precision for predicting images that are normal.

Recall for images that are indicative of PTB was 0.86 % and 0.94% for normal images. The F1-score, which is the harmonic mean of the precision and recall, where it reaches its best value as it get closer to 1 (perfect precision and recall) was found to be 0.90 % for images that are indicative of PTB and 0.91% for normal images. This is shown in table 41 and with confusion matrix in figure 32.

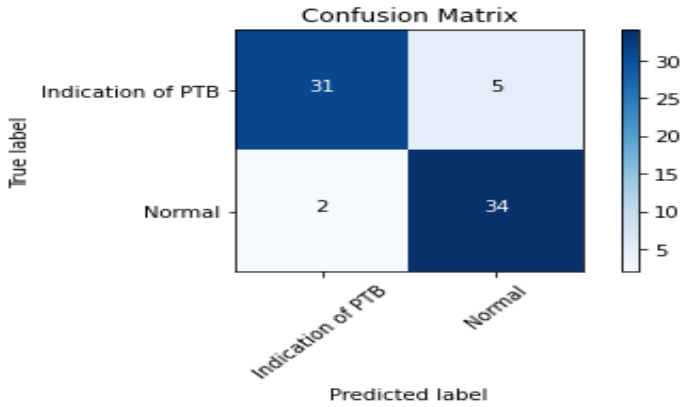


Figure 32: Confusion Metrics of the validation data.

Table 41: Precision, Recall and F1-score of the validation data.

	Precision	Recall	F1-score	Support
Indication of PTB	0.94	0.86	0.90	36
Normal	0.87	0.94	0.91	36
Accuracy			0.90	72
Macro avg	0.91	0.90	0.90	72
Weighted avg	0.91	0.90	0.90	72

After the model was trained and good validation accuracy with low loss value was achieved as shown with the classification report in table 41, the model prediction performance on new images was evaluated by using the test data. The test data contains 80 images. Because the images were pre-labeled, the predictions of the system can easily be compared with the true labels. Sample of the comparison made between the models prediction and the true labels of the test images is shown in table 42.

Table 42: Comparison of system's prediction with images' true labels.

Image id	System prediction	True label
MCUCXR_0094	Normal	Normal
MCUCXR_0101	Normal	Normal
CHNCXR_0278	Indication of PTB	Normal
CHNCXR_0280	Normal	Normal
CHNCXR_0283	Normal	Normal
MCUCXR_0338	Indication of PTB	Indication of PTB
MCUCXR_0399	Indication of PTB	Indication of PTB
CHNCXR_0613	Indication of PTB	Indication of PTB
CHNCXR_0615	Normal	Indication of PTB
CHNCXR_0618	Indication of PTB	Indication of PTB

Confusion matrix was used over the test data to find the true positive, true negative, false positive and false negative predictions of the model as shown in figure 33.

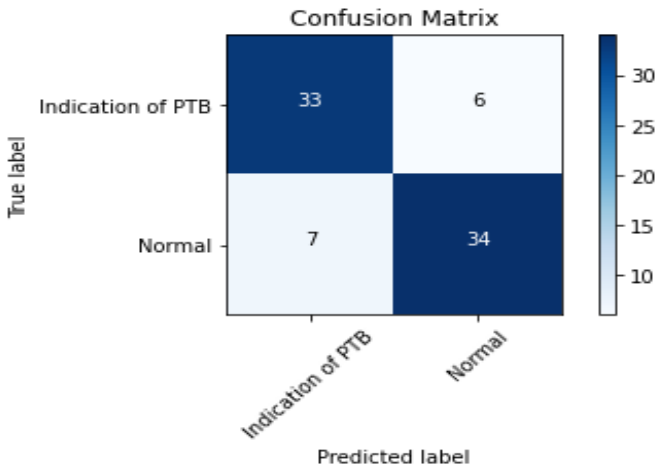


Figure 33: Confusion Metrics of the test data.

When translating the output of the model to Normal or Abnormal, the predicted result could be compared to actual result and summarized as follows [112]:

- True Positives (TP): is an outcome where the actual and predicted transactions were Abnormal
- True Negatives (TF): is an outcome where the actual and predicted transactions were Normal
- False Positives (FP): is an outcome where the actual transactions were Normal but predicted to be Abnormal
- False Negatives (FN): is an outcome where the actual transactions were Abnormal but were predicted to be Normal

Table 43: The chest X-ray classification model prediction.

	Predictions values					
	TP	**TN**	**FP**	**FN**	**Execution time per image (after system start running)**	**No. of images**
✓ ***System prediction***	33	34	7	6	1:15 min	80

The prediction scores of the classification model that are shown in table 43 were then used to calculate the accuracy, sensitivity and specificity of the model.

Metrics used for testing the classification model

- Accuracy - is the fraction of predictions a model got right [112].

$$\frac{TP + TN}{TP + TN + FP + FN}$$

- Sensitivity - is the proportion of real positive cases that are correctly predicted positive [112].

$$\frac{TP}{TP + FN}$$

- Specificity - relates to the classifier's ability to identify negative results. Measures the proportion of actual negatives that are correctly identified [112].

$$\frac{TN}{TN + FP}$$

- Precision - precision or confidence denotes the proportion of predicted positive cases that are correctly real positives [112].

$$\frac{TP}{TP + FP}$$

Table 44: Sensitivity, specificity and precision of the system.

	Accuracy	Sensitivity	Specificity	Precision
Chest X-ray image classification model	**0.84**	**0.85**	**0.83**	**0.83**

Finally, by using the prediction level of the system from the confusion matrix, the sensitivity, specificity and precision of the system were calculated. As shown in table 44, the model's accuracy is 84% which is encouraging. By incorporating the chest X-ray image classification model as one examination modality for PTB, the designed expert system would be of great assistance to medical practitioners.

In general, the designed expert system's accuracy is remarkable. From the 20 patients' data used for testing, 18 were correctly diagnosed by the system. Unlike the existing expert systems for the diagnosis of TB, by using more suggestive symptoms, analysing symptoms first to narrow down disease suspicion level, and finally by applying very effective diagnostic modalities, the system accuracy was made to increase. The main objective of the research, which is making TB diagnosis more accurate by focusing on the main area causing the problem which is in the diagnosis of EPTB, is fulfilled. The chest X-ray image classification could have given a better accuracy than the one achieved if the data used for training was increased and local chest X-ray was included. But due to lack of dataset in the research areas, only online datasets were applied.

5.2 Discussion

In developing countries, apart from other causes that have contributed to the poor health care service, inadequate number of well experienced medical professionals plays a major role. This makes it hard to provide sufficient number of well experienced health care providers over the rural areas where the larger proportion of the society is located.

In this research, it is well reflected that designing a system which will assist medical personnel especially with less experience in specific fields is the key to solve the problem of inadequacy in the number of well-educated and experienced medical professionals in developing countries. Assisting non-experts from symptom analysis to ordering specific and most indicative diagnosis modalities to the medication prescription at expert's level is the best way to make sure accurate, timely diagnosis and treatment of patients.

Bearing in mind the above mentioned problems in developing countries, this research was conducted to provide a design solution. In the research, the first step in disease diagnosis that is patient's symptom analysis is performed by using fuzzy expert system. Fuzzy expert systems with their capability of dealing with imprecise and vague inputs and the transparent relationship they provide between the input and output makes them the best candidate for the task. In the first step of the fuzzy expert system, which is fuzzification of the input values, as shown in figure 16 and 17, triangular membership function was chosen by the three expert doctors because it provided an acceptable output. From the three commonly known methods of inference, mamdani was applied which differs from the other two when the results of all rules are integrated into a single precise value [32]. Mamdani is straight forward and contains defuzzification of the fuzzy sets to a single output which is understandable by the user [32]. Finally, due to the consistency seen in its results, its excellent performance [39], [40] and its acceptable output by the domain experts as shown in table 11, the center of gravity was used to defuzzify the fuzzy output After the suspicion level of each of the diseases was found by using the fuzzy expert system, the research proceeded to ordering examination modalities for the highly suspected ones, therefore providing the user with a full TB diagnosis. The examination finding analysis was made by using rule based expert system which has incredible performance in generalizing by using previous personal experiences and captures the reasoning capacity of humans.

Apart from the fuzzy and rule based hybrid TB diagnosis assistive expert systems, chest X-ray classification as one examination modality for the diagnosis of PTB was also incorporated in the system to increase its problem solving ability. ResNet 50, a pre-trained convolutional neural network was used on two commercial datasets to build the chest X-ray classification model. On the other hand, to solve the problem with the manual patient data recording system especially for TB patients whose treatment takes a minimum of 6 months, a database was also designed using Microsoft SQL server.

By applying fuzzy and rule based expert systems on carefully chosen symptoms and examination modalities with the help of the expert doctors, a very good system accuracy of 0.933 was achieved. This achievement is better than the works that used fuzzy and rule based expert systems independently [53] - [58] and a comparable result was also achieved when compared with literatures [51], [52] that used ANN. The chest X-ray image classification model attained an accuracy of 0.84, a sensitivity of 0.85, a specificity of 0.83 and a precision of 0.83. Furthermore, an interactive user interface and a database for recording patient data were also successfully designed. If this research is viewed from an angle of solving the problems of developing countries, which is the main goal of this research, it most definitely will be the best choice of all.

Predictive models have not fared much better in solving the problems of developing countries. A review of the literatures revealed only a handful of studies that have attempted to tackle this problem. As stated earlier, comparing the results of this study with Temurtas et.al [51] and Serghani et.al [52], comparable classification accuracy was achieved. However, the designed expert system by considering the low availability of experienced medical professionals, and by considering the user as a non-expert and assisting him/her through the diagnosis of TB and its major classifications, a very compelling result was achieved which has a potential of solving the problem better than the two mentioned works.

The unquantified accuracy achieved by the three fuzzy expert systems [53], [54] and [55] is tremendously outdone by incorporating rule based expert system for analysing different diagnostic examination findings and achieving system accuracy of 0.933. In addition to the accuracy level achieved by the designed system, the other features which are added such as chest X-ray classification model as one of the examination modalities for PTB, medication prescription and database for patient data recording increased system importance and problem solving capacity extensively.

The belief rule based expert system [57] which has tried to improve the ability of such systems in dealing with imprecise and vague inputs is outweighed by the designed expert system by a value of 0.023 system accuracy.

The work in Adewole et al. [56] and Kulkarni et al. [58] use rule based expert systems to deal with vague inputs like patients' symptoms and do not include examination to reach at diagnosis results which creates questionable system accuracy. Furthermore, literature [58] does not consider the technological, economic and educational level of the larger society of developing countries.

This research, unlike Adewole et al. [56] and Kulkarni et al. [58], by using fuzzy expert system for analysing patient symptoms and rule based expert system for assessing examination finding and finally prescribing the patient with the right medication, helps a non-expert user to accomplish TB diagnosis at expert's level and gives a better performance, accuracy and most of all solves the problem of inadequate number of experienced medical professionals in developing countries.

Comparisons of different research results and the result of this research are presented in table 45. Different paper results are presented with the input features they used, the diseases they are designed to diagnose, additional features they added other than prediction of disease suspicion level and the level of accuracy they acquired.

Table 45: Comparative analysis of this research with different works of literature.

Papers	Features used as input	Diseases system diagnose	Additional features other than disease suspicion level prediction	Accuracy (%)
TB disease diagnosis using artificial neural network[51]	38 (Symptoms & tests)	PTB	Diagnostic examinations	0.95
Predicting active pulmonary TB using artificial neural network [52]	20 (Symptoms & tests)	PTB	Diagnostic examinations	0.923
Diagnostics decision support system for TB using fuzzy logic [53]	10 (Symptoms)	PTB	-	Acceptable
Fuzzy cluster means expert system for the diagnosis of tuberculosis [54]	20 (Symptoms)	Seven forms of TB does not include PTB	-	Acceptable
Efficient fuzzy-based system for the diagnosis and treatment of TB [55]	18 (Symptoms)	Five forms of TB including PTB	Medication prescription	Acceptable
Rule-based expert system for disease diagnosis [56]	46 (Symptoms)	Malaria, typhoid Fever, cholera, TB and breast cancer	-	Acceptable
A belief rule based expert system to assess TB under uncertainty [57]	8 (Symptoms)	PTB	-	0.910
Expert system for clinical diagnosis of TB (Android application) [58]	10 (Symptoms & a test)	PTB	One suggestive examination Mobile application	-
This paper	5 or less symptoms and 4 examinations for each diseases	PTB, pneumonia, asthma, COPD, TB of osteo-articular, TB of GIT, TB of meninges and TB of lymph-node	Diagnostic examinations, Medication prescription, Chest X-ray classification model & Database for patient data recording	0.933

CHAPTER SIX

Conclusion and Recommendation

6.1 Conclusion

In the research, a decision support system which applies both fuzzy and rule-based types of expert systems was designed using python programing language for the accurate diagnosis of TB. In the fuzzy expert system, triangular membership function, mamdani fuzzy inference mechanism and center of gravity defuzzification techniques were applied. The methods applied were chosen by reviewing different literatures which compare and contrast their performance, and by analysing their applicability and the desired output of the system with the help of medical doctors.

The fuzzy expert system was applied to diagnose patients' symptoms and determine the suspicion level of each disease in order to run examination. To determine the final diagnosis result of the patient, rule-based expert system was applied. In this portion of the designed system, different examination modalities with the highest capabilities of indicating the presence or absence of each disease were chosen. Rules were formulated by using the chosen examinations modalities and their respective outcomes.

After the final diagnosis result is determined, medication is prescribed for the diagnosed disease. The choice of the medications was as recommended by WHO and as being used in Ethiopia in the current diagnosis of TB. Overall system accuracy of 93% was achieved by the fuzzy and rule based hybrid expert system.

As one of the examination modalities for the diagnosis of PTB, the chest X-ray classification is made by the system. To design the image classification model, ResNet50 convolutional neural network architecture was used. This CNN architecture was chosen due to its ability to train deep layers with high accuracy level without losing its integrity and performance. Two online data set sources were used to train the model. The classification model achieved a good accuracy level of 84%.

The user interface was designed by using visual studio. This integrated development environment was very helpful in making the interface very user-friendly and easily accessible.

To solve the problem with the current patient diagnosis data recording system, the designed system also integrates a computerized data recording system which increases system usefulness even more. Patients' registration information, symptom complaints, final diagnosis results and medication prescription are saved in the database.

The database was designed by using SQL server. Since TB treatment takes a long time, the database will be helpful to follow the patients' progress throughout the treatment. Examinations performed in the middle of the treatment for checking patients' recovery are also saved in the system for easy access.

Finally, the attempt of designing a full decision support system for the accurate diagnosis of TB succeeded with promising and encouraging results. This design will contribute a great deal in making the diagnosis of TB more accurate and will pave the way for better assistive expert systems to be built in the future for developing countries. This will increase the quality of the health care service which is suffering from disproportionate number of human experts in many fields.

6.2 Recommendation

Tuberculosis continues to be a big threat for developing countries. The best solution to overcome this problem is to continue with the development of expert systems. Expert systems, with their high accuracy level, low user knowledge requirement and remarkable reduction of diagnosis delay will become the best possible solution for developing countries like Ethiopia. In order to make this expert system functionality exquisite, the participation of medical personnel as a team with biomedical engineers and all the necessary departments is very crucial since their knowledge is the base for the existence of expert systems. Finally, the government needs to draw its focus on such systems as they can solve not only medical problems, but so much more.

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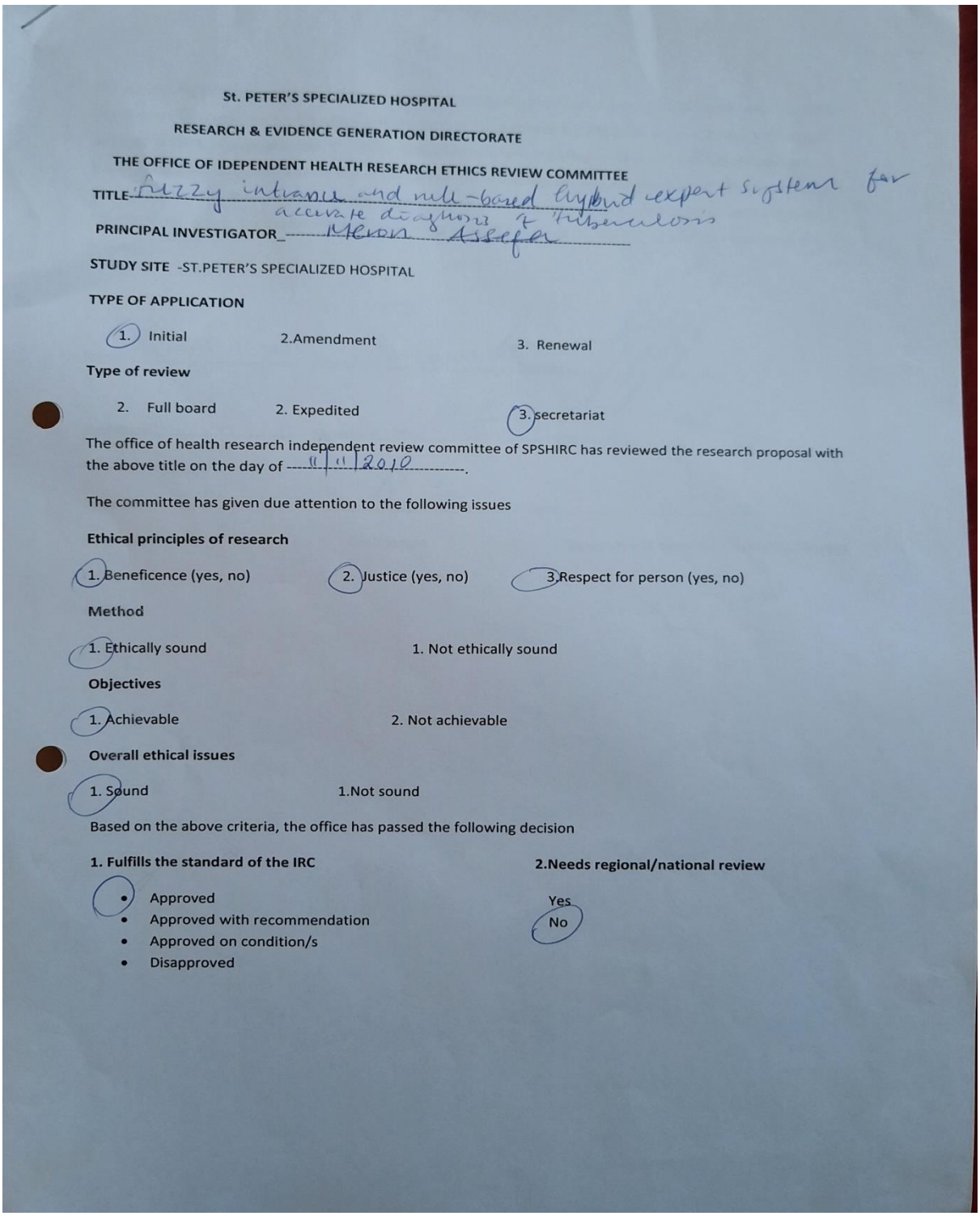
APPENDIX

I) Letter from St. Peter's Specialized Hospital



ST. PETER'S SPECIALIZED HOSPITAL

RESEARCH & EVIDENCE GENERATION DIRECTORATE

THE OFFICE OF IDEPENDENT HEALTH RESEARCH ETHICS REVIEW COMMITTEE

TITLE- Fuzzy intranet and rule-based hybrid expert system for accurate diagnosis of Tuberculosis

PRINCIPAL INVESTIGATOR_ Meron Asefa

STUDY SITE -ST.PETER'S SPECIALIZED HOSPITAL

TYPE OF APPLICATION

1. Initial 2.Amendment 3. Renewal

Type of review

2. Full board 2. Expedited 3. secretariat

The office of health research independent review committee of SPSHIRC has reviewed the research proposal with the above title on the day of 11/11/2020.

The committee has given due attention to the following issues

Ethical principles of research

1. Beneficence (yes, no) 2. Justice (yes, no) 3.Respect for person (yes, no)

Method

1. Ethically sound 1. Not ethically sound

Objectives

1. Achievable 2. Not achievable

Overall ethical issues

1. Sound 1.Not sound

Based on the above criteria, the office has passed the following decision

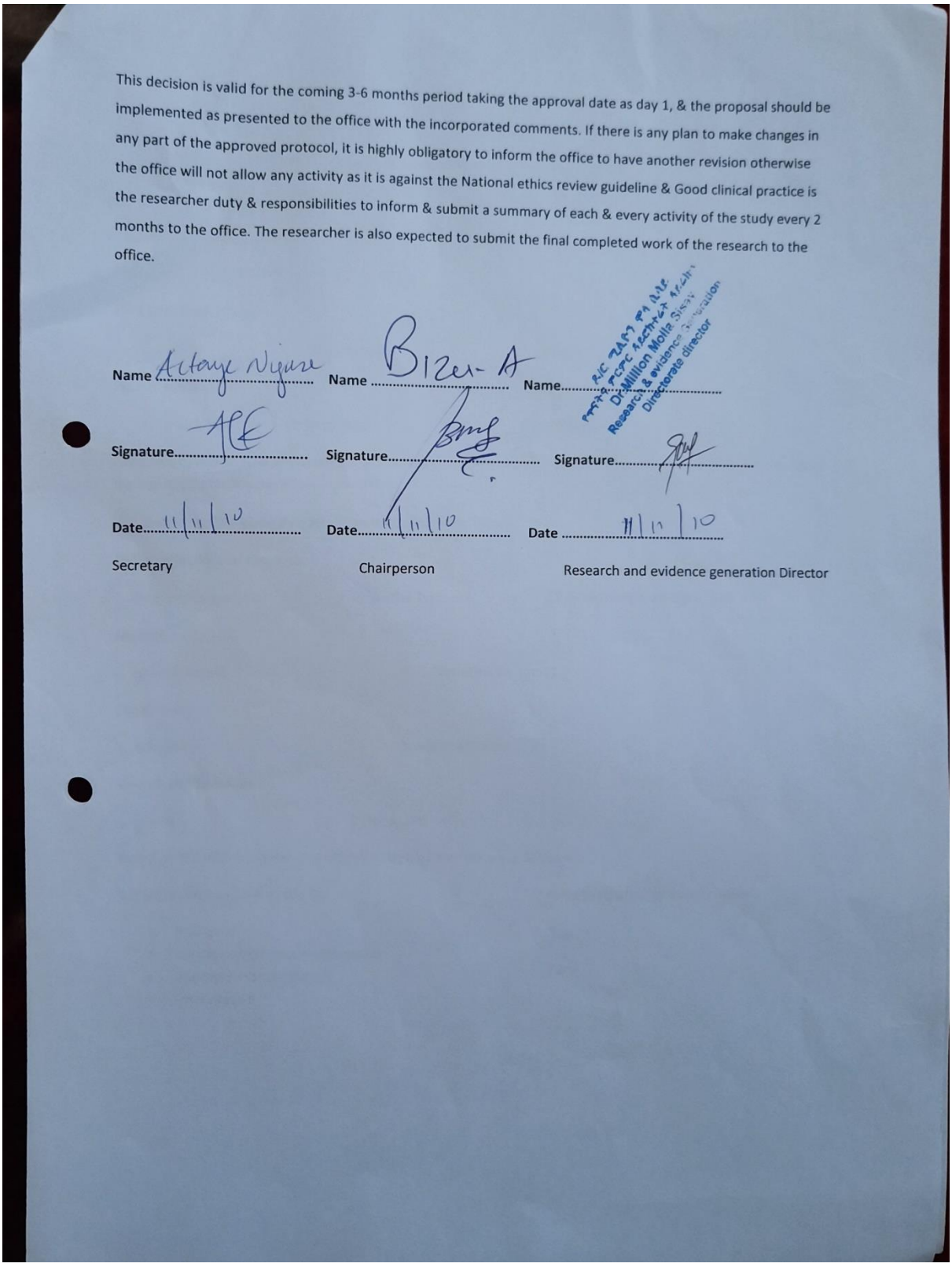
1. Fulfills the standard of the IRC

- Approved
- Approved with recommendation
- Approved on condition/s
- Disapproved

2.Needs regional/national review

Yes

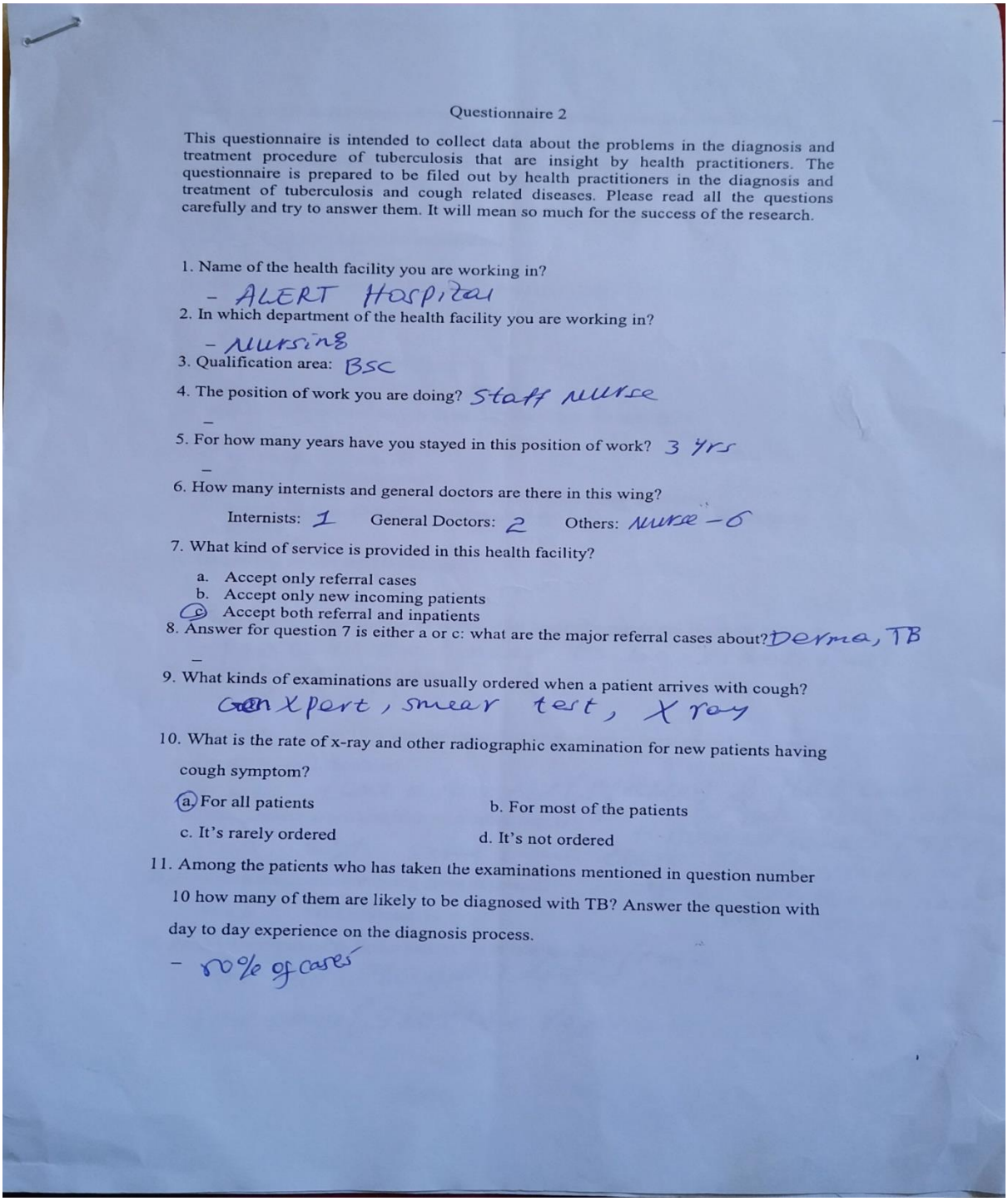
No



This decision is valid for the coming 3-6 months period taking the approval date as day 1, & the proposal should be implemented as presented to the office with the incorporated comments. If there is any plan to make changes in any part of the approved protocol, it is highly obligatory to inform the office to have another revision otherwise the office will not allow any activity as it is against the National ethics review guideline & Good clinical practice is the researcher duty & responsibilities to inform & submit a summary of each & every activity of the study every 2 months to the office. The researcher is also expected to submit the final completed work of the research to the office.

Name Actaye Nigus	Name Bizu A	Name Dr Million Molla Research & evidence generation Directorate director
Signature	Signature	Signature
Date 11/11/10	Date 11/11/10	Date 11/11/10
Secretary	Chairperson	Research and evidence generation Director

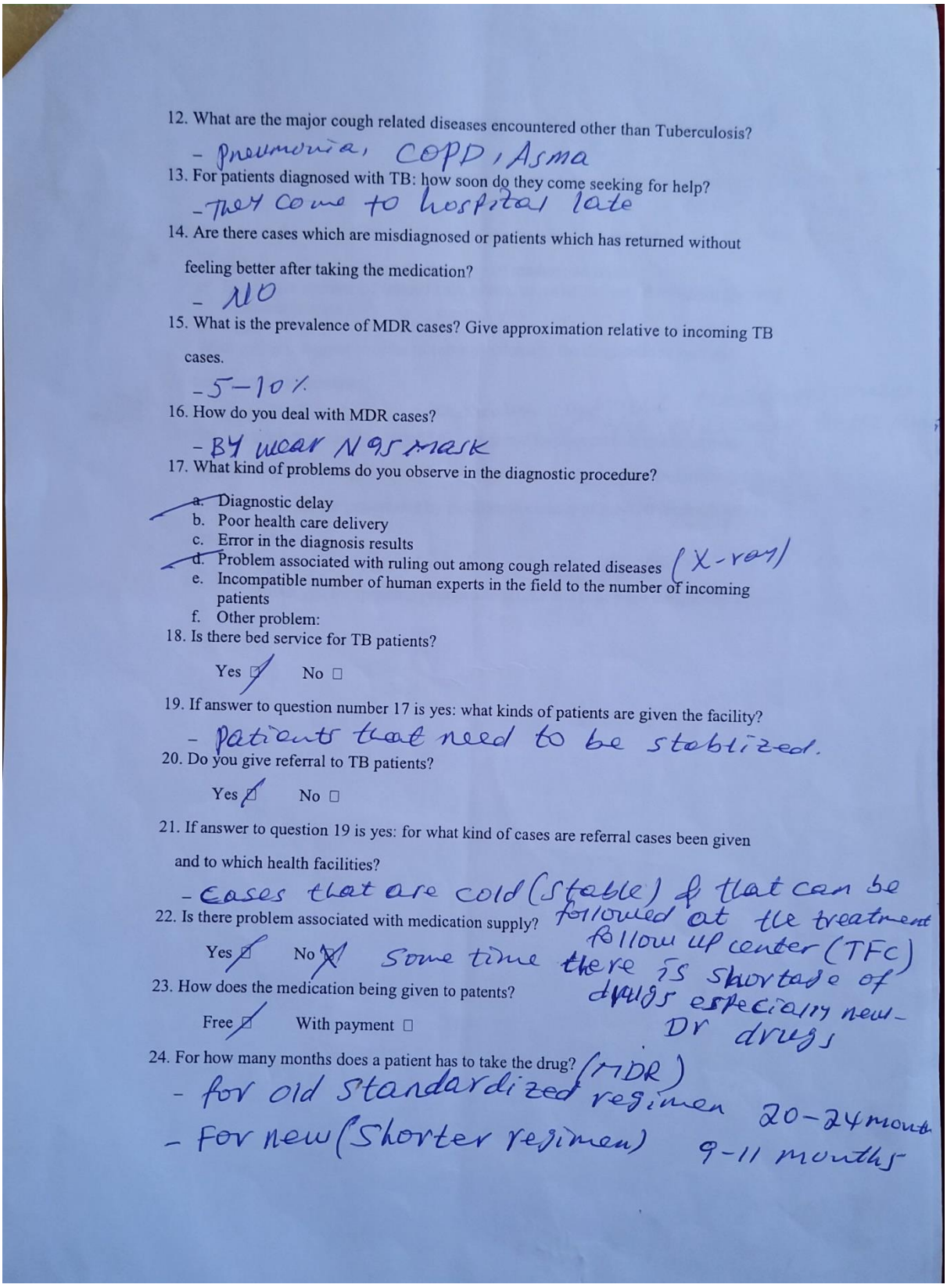
II) A questionnaire prepared to be filled out by nurses working in TB OPD in order to find TB mimicking cough related disease, the type of examinations ordered for the diagnosis of PTB and the treatment regimen of TB among other questions



Questionnaire 2

This questionnaire is intended to collect data about the problems in the diagnosis and treatment procedure of tuberculosis that are insight by health practitioners. The questionnaire is prepared to be filed out by health practitioners in the diagnosis and treatment of tuberculosis and cough related diseases. Please read all the questions carefully and try to answer them. It will mean so much for the success of the research.

1. Name of the health facility you are working in?
   - ALERT Hospital
2. In which department of the health facility you are working in?
   - Nursing
3. Qualification area: BSc
4. The position of work you are doing? Staff nurse
5. For how many years have you stayed in this position of work? 3 yrs
6. How many internists and general doctors are there in this wing?
   Internists: 1 General Doctors: 2 Others: nurse – 6
7. What kind of service is provided in this health facility?
   a. Accept only referral cases
   b. Accept only new incoming patients
   c. Accept both referral and inpatients
8. Answer for question 7 is either a or c: what are the major referral cases about? Derma, TB
9. What kinds of examinations are usually ordered when a patient arrives with cough?
   Gen Xpert, smear test, X ray
10. What is the rate of x-ray and other radiographic examination for new patients having cough symptom?
    a. For all patients
    b. For most of the patients
    c. It's rarely ordered
    d. It's not ordered
11. Among the patients who has taken the examinations mentioned in question number 10 how many of them are likely to be diagnosed with TB? Answer the question with day to day experience on the diagnosis process.
    - 80% of cases



12. What are the major cough related diseases encountered other than Tuberculosis?
- Pneumonia, COPD, Asma
13. For patients diagnosed with TB: how soon do they come seeking for help?
- They come to hospital late
14. Are there cases which are misdiagnosed or patients which has returned without feeling better after taking the medication?
- NO
15. What is the prevalence of MDR cases? Give approximation relative to incoming TB cases.
- 5–10%
16. How do you deal with MDR cases?
- By wear N95 mask
17. What kind of problems do you observe in the diagnostic procedure?

a. Diagnostic delay
b. Poor health care delivery
c. Error in the diagnosis results
d. Problem associated with ruling out among cough related diseases (X-ray)
e. Incompatible number of human experts in the field to the number of incoming patients
f. Other problem:

18. Is there bed service for TB patients?

Yes ☑ No ☐

19. If answer to question number 17 is yes: what kinds of patients are given the facility?
- patients that need to be stabilized.
20. Do you give referral to TB patients?

Yes ☑ No ☐

21. If answer to question 19 is yes: for what kind of cases are referral cases been given and to which health facilities?
- Cases that are cold (stable) & that can be followed at the treatment follow up center (TFC)
22. Is there problem associated with medication supply?

Yes ☑ No ☒ Some time there is shortage of drugs especially new-DR drugs

23. How does the medication being given to patents?

Free ☑ With payment ☐

24. For how many months does a patient has to take the drug? (MDR)
- for old standardized regimen 20–24 months
- For new (Shorter regimen) 9–11 months

25. Are there major problems with patients forgetting there medication intake? NO

26. What kind of methods do you use to make patients remember their medications? they may use Alarm,

27. What kind of problems do you observe in the treatment procedure?

a. Patients orientation about the disease and medication intake
b. Inadequate number of trained care givers to assist patients throughout the long treatment process
c. Other:

28. What will you suggest in order to solve problems in the diagnostic as well as treatment of tuberculosis?

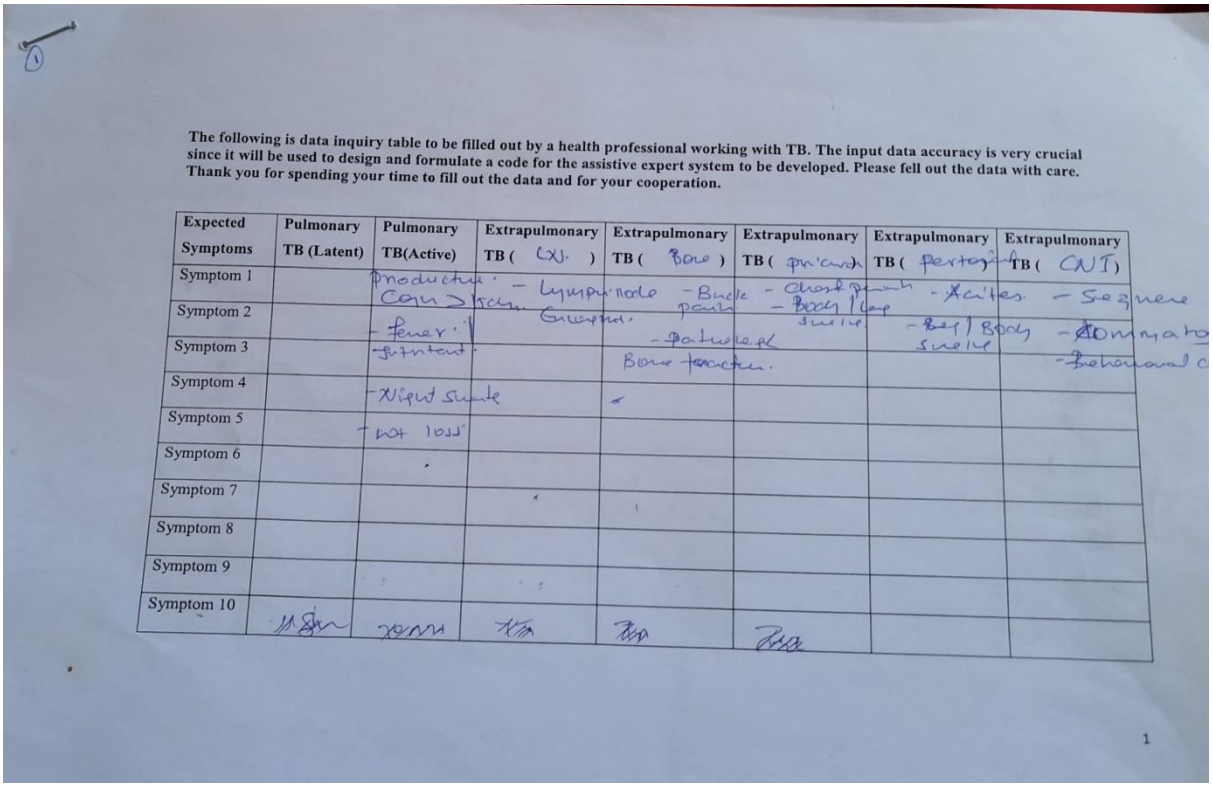
- Awareness creation about the dangerousness of the disease to the public

29. Do you think that it will be helpful to design and implement a decision support system for accurate diagnosis of TB and major mimicking diseases by reducing the work load and fill the gap created by inadequate number of medical professionals in the country?

- if it is feasible, it is a wonderful idea.

Thank you for spending your precious time and filling out the questionnaire.

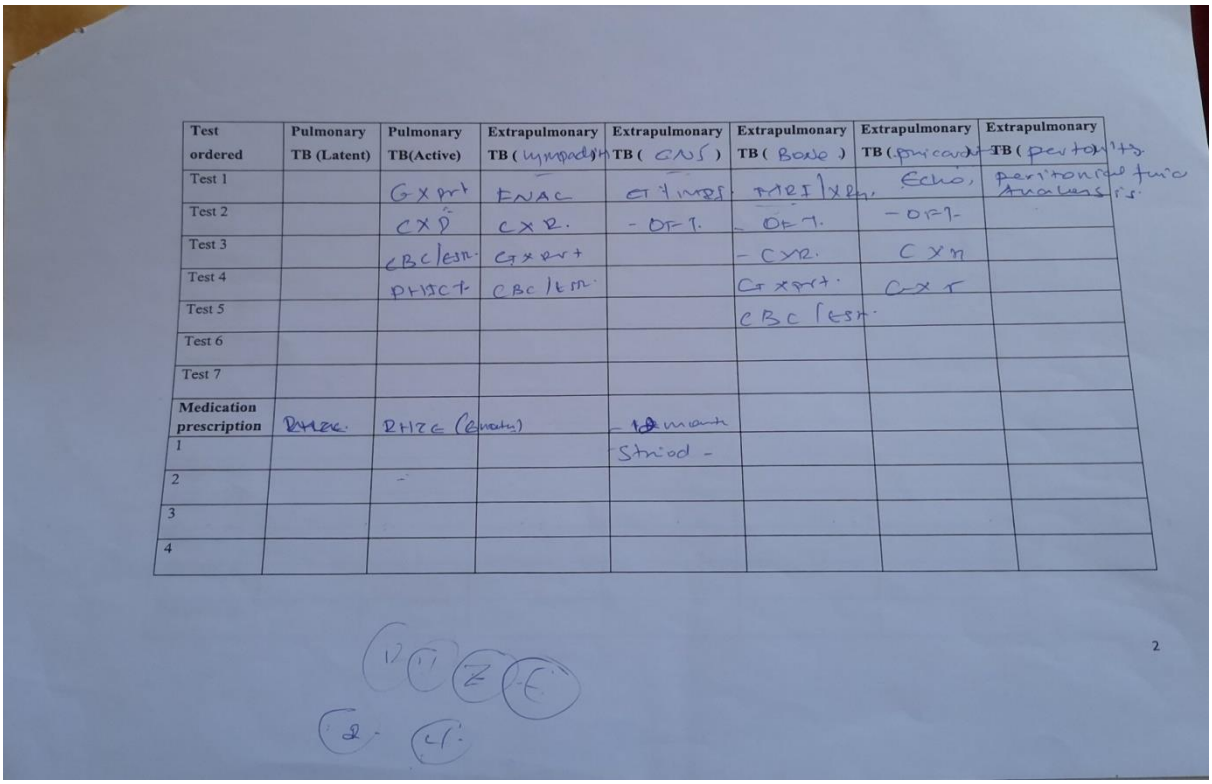
III) A form to be filled out by doctors in the field of TB diagnosis to acquire symptoms of cough related diseases and EPTB diseases with their specific examination modalities



The following is data inquiry table to be filled out by a health professional working with TB. The input data accuracy is very crucial since it will be used to design and formulate a code for the assistive expert system to be developed. Please fell out the data with care. Thank you for spending your time to fill out the data and for your cooperation.

Expected Symptoms	Pulmonary TB (Latent)	Pulmonary TB(Active)	Extrapulmonary TB (LN)	Extrapulmonary TB (Bone)	Extrapulmonary TB (pericard)	Extrapulmonary TB (perito)	Extrapulmonary TB (CNT)
Symptom 1		Productive Cough	- lymph node Enlargment	- Bone pain	- Chest pain - Body / leg swelling	- Ascites	- Seizure
Symptom 2		- fever				- Bag / Body swelling	- Abnormal
Symptom 3		- fatigue		- Pathological Bone fracture			- Behavioral c
Symptom 4		- Night sweate					
Symptom 5		- Hot loss					
Symptom 6							
Symptom 7							
Symptom 8							
Symptom 9							
Symptom 10							

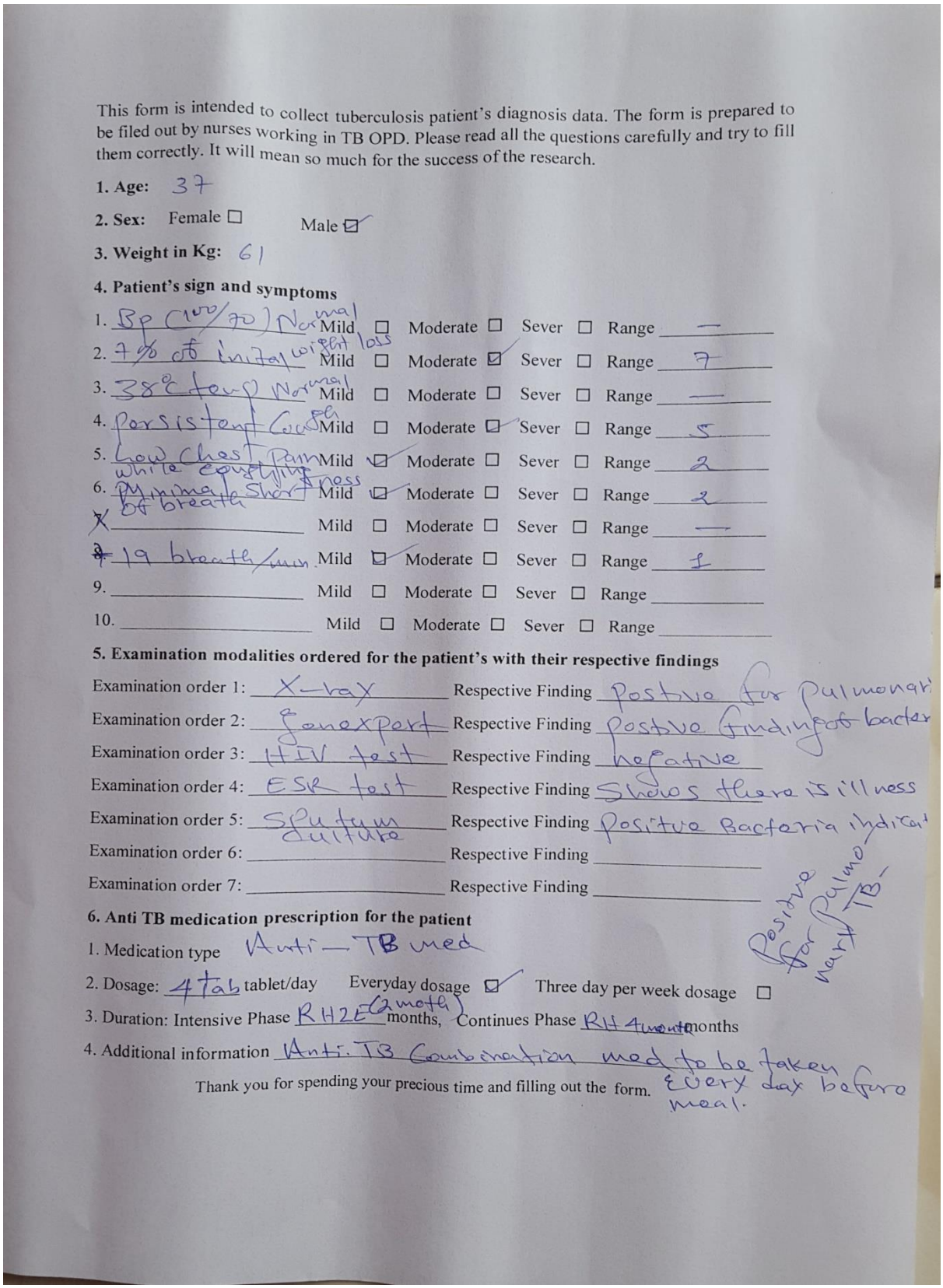
1



Test ordered	Pulmonary TB (Latent)	Pulmonary TB(Active)	Extrapulmonary TB (lymph)	Extrapulmonary TB (CNS)	Extrapulmonary TB (Bone)	Extrapulmonary TB (pericard)	Extrapulmonary TB (perito)
Test 1		GXpert	FNAC	CT / MRI	MRI / XR	Echo,	peritoneal fluid Analysis
Test 2		CXR	CXR	- OFT	- OFT	- OFT	
Test 3		CBC/ESR	GXpert		- CXR	CXR	
Test 4		PHYCT	CBC/ESR		GXpert	CXT	
Test 5					CBC/ESR		
Test 6							
Test 7							
Medication prescription		RHZE (equity)		- Steroid -			
1							
2							
3							
4							

2

IV) Patient diagnosis data collection form



This form is intended to collect tuberculosis patient's diagnosis data. The form is prepared to be filed out by nurses working in TB OPD. Please read all the questions carefully and try to fill them correctly. It will mean so much for the success of the research.

1. Age: 37

2. Sex: Female ☐ Male ☑

3. Weight in Kg: 61

4. Patient's sign and symptoms

1. Bp (100/70) Normal — Mild ☐ Moderate ☐ Sever ☐ Range —
2. 7% of initial weight loss — Mild ☐ Moderate ☑ Sever ☐ Range 7
3. 38°c temp Normal — Mild ☐ Moderate ☐ Sever ☐ Range —
4. Persistent Cough — Mild ☐ Moderate ☑ Sever ☐ Range 5
5. Low Chest Pain while coughing — Mild ☑ Moderate ☐ Sever ☐ Range 2
6. Shortness of breath — Mild ☑ Moderate ☐ Sever ☐ Range 2
7. _____ — Mild ☐ Moderate ☐ Sever ☐ Range —
8. 19 breath/min — Mild ☑ Moderate ☐ Sever ☐ Range 1
9. _____ — Mild ☐ Moderate ☐ Sever ☐ Range _____
10. _____ — Mild ☐ Moderate ☐ Sever ☐ Range _____

5. Examination modalities ordered for the patient's with their respective findings

Examination order 1: X-ray — Respective Finding Postive for Pulmonary
Examination order 2: GeneXpert — Respective Finding Postive finding of bacter
Examination order 3: HIV test — Respective Finding negative
Examination order 4: ESR test — Respective Finding Shows there is illness
Examination order 5: Sputum culture — Respective Finding positive Bacteria indicat
Examination order 6: _____ — Respective Finding _____
Examination order 7: _____ — Respective Finding _____

Positive for Pulmonary TB

6. Anti TB medication prescription for the patient

1. Medication type Anti-TB med
2. Dosage: 4 tab tablet/day Everyday dosage ☑ Three day per week dosage ☐
3. Duration: Intensive Phase RHZE (2 months) months, Continues Phase RH 4 months months
4. Additional information Anti. TB Combination med to be taken every day before meal.

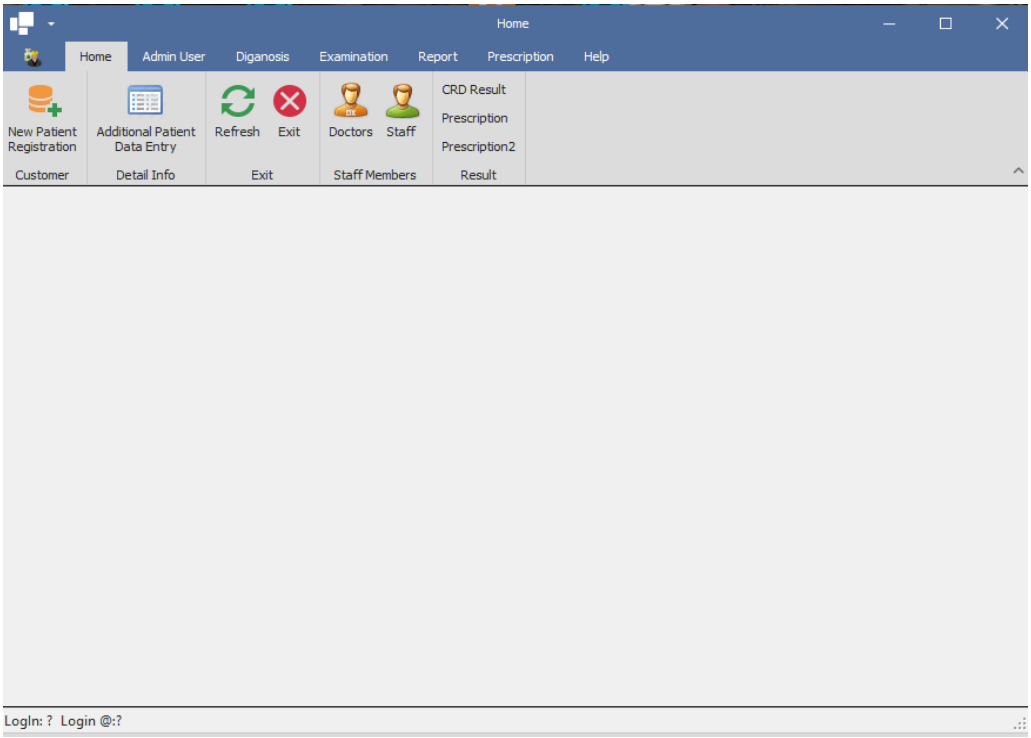
Thank you for spending your precious time and filling out the form.

V) User guide for the designed fuzzy and rule based hybrid expert system

- **The login form**

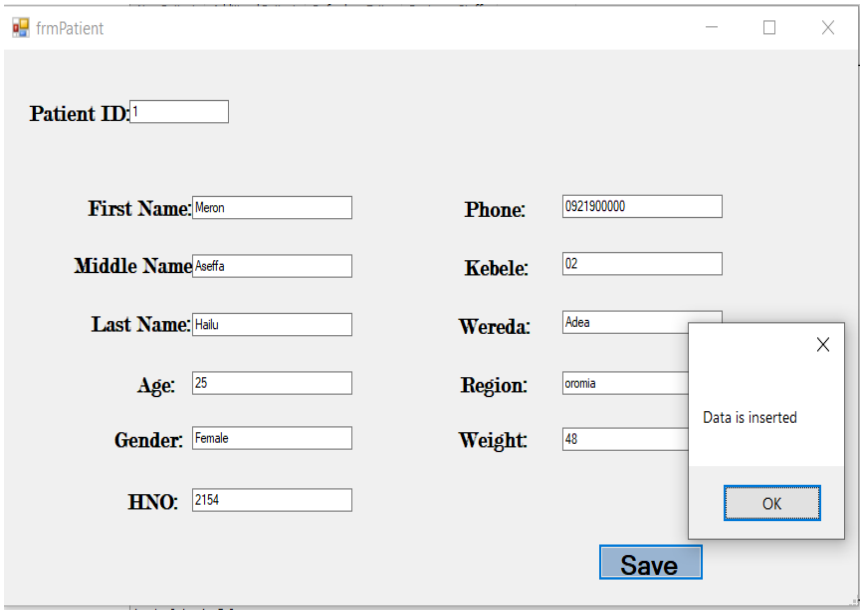
The login gives different health professionals different authorization since their access point differs.

- **Main window of the expert system**

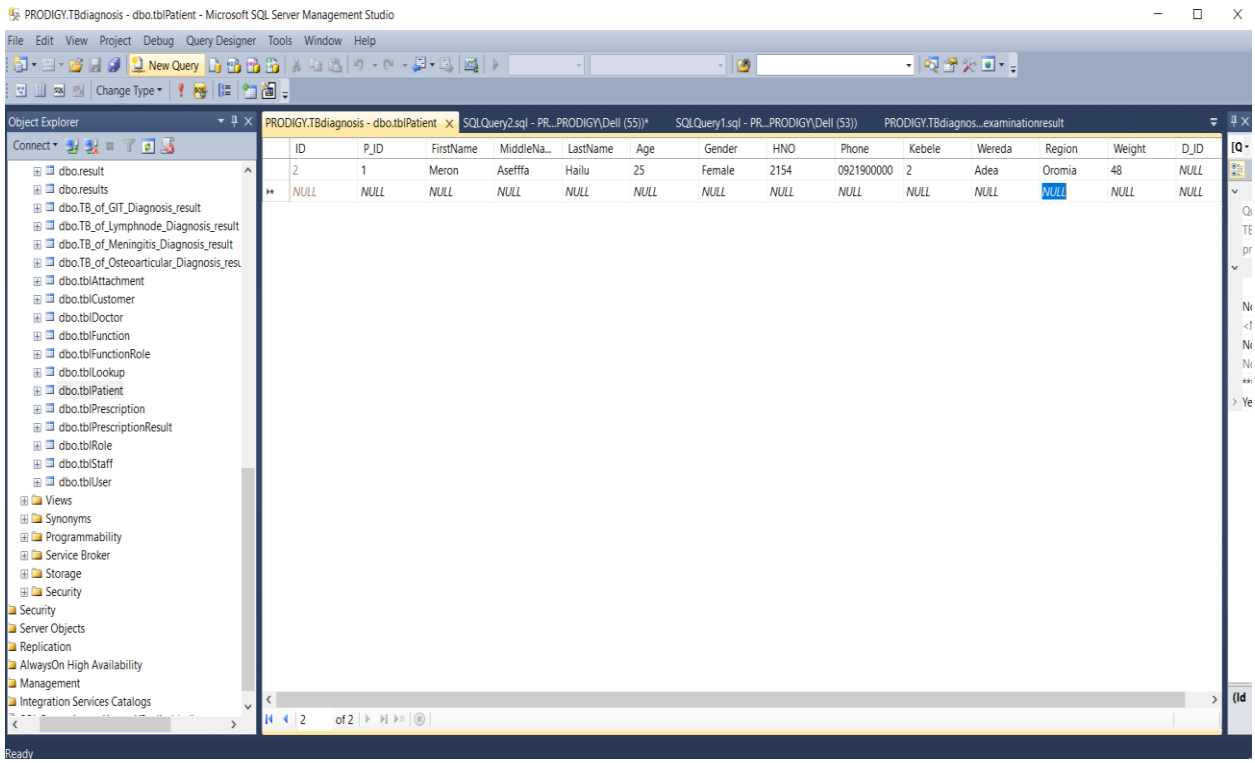


After authorization is confirmed, the main window shown in the above figure will be displayed for the user to choose a task.

- **Step 1: Patient registration form**

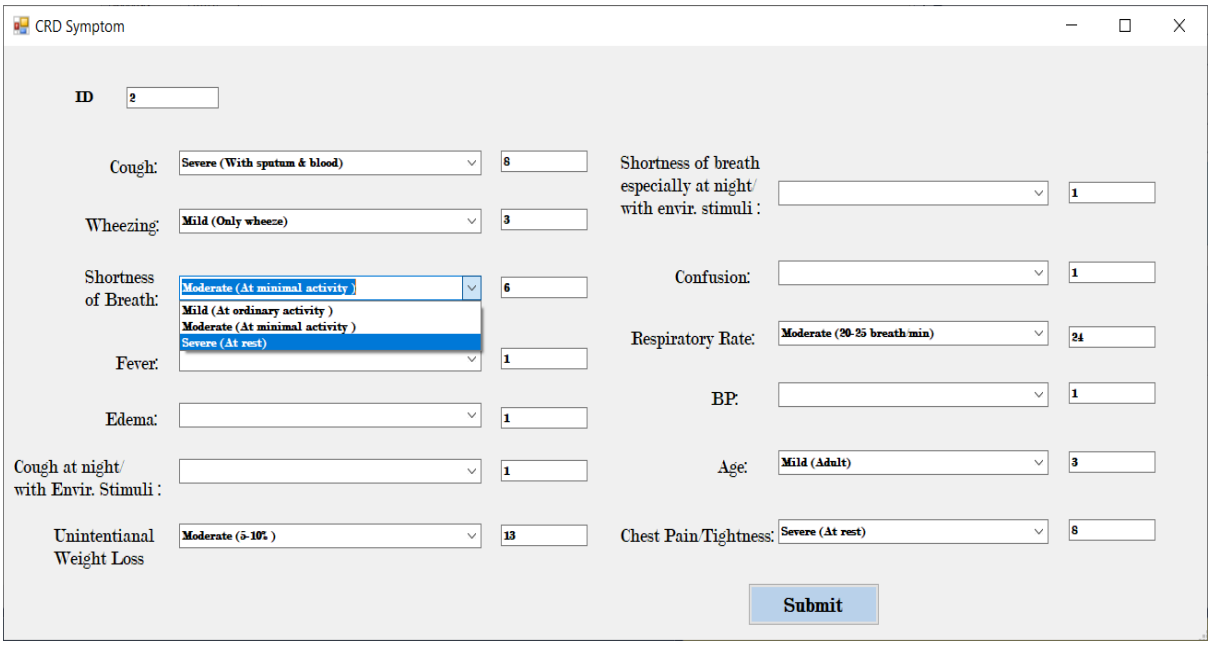


- **Patient registration data saved in the database (SQL server)**

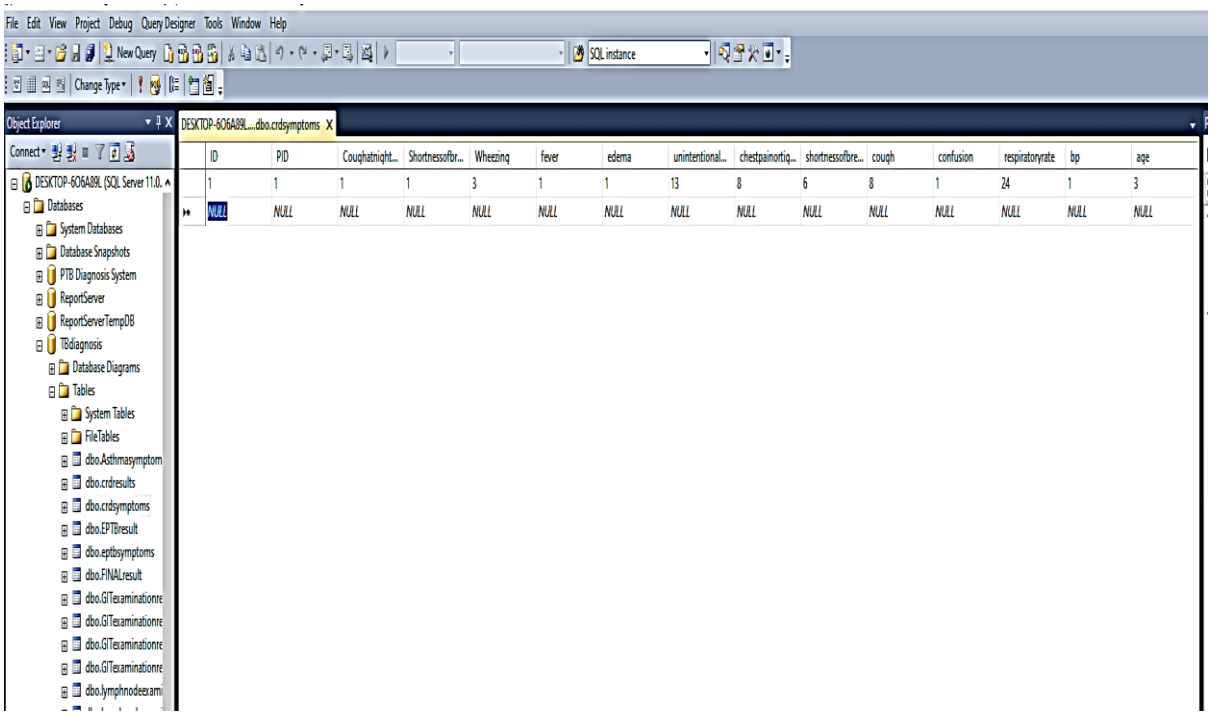


If new patient registration is chosen, the window in **Step 1** will pop up for the user to insert data and this data will be saved on the database as shown in the above figure.

- **Step 2: Symptom collection form**

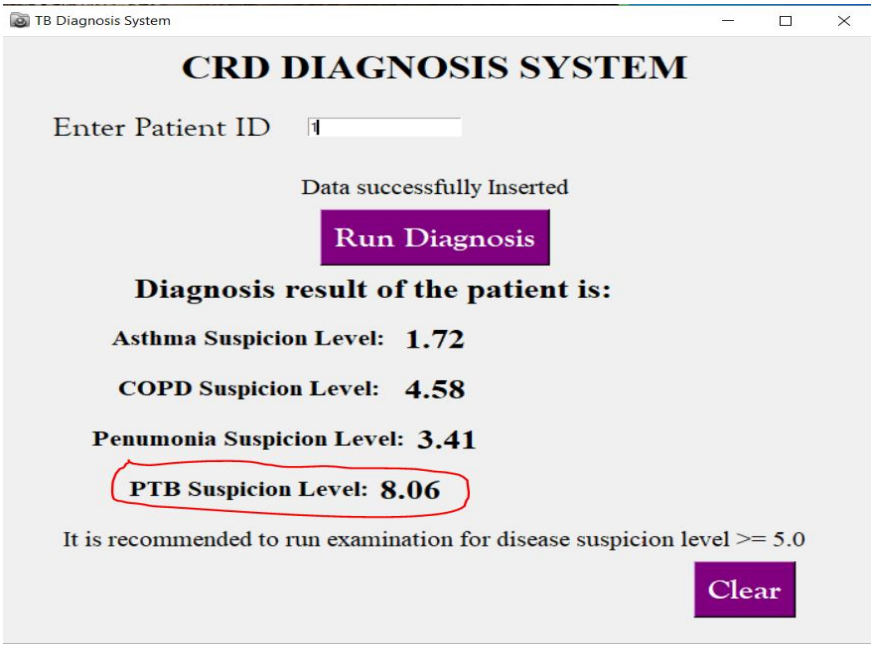


- **Database where patient symptoms are saved**



Once the registration is done, based on the registered patient's identification number, the symptoms experienced by the patient will be fed to the system and saved on database as shown in **Step 2**.

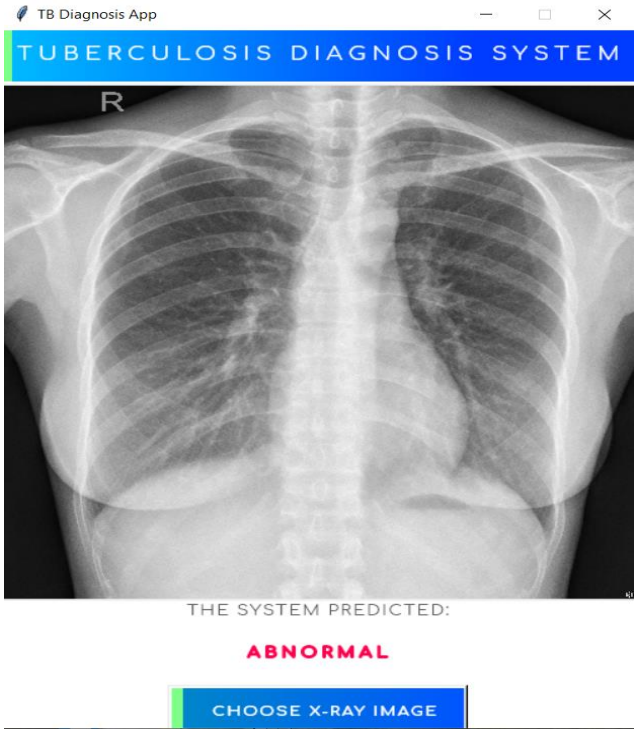
- **Step 3: Examination for cough related diseases**



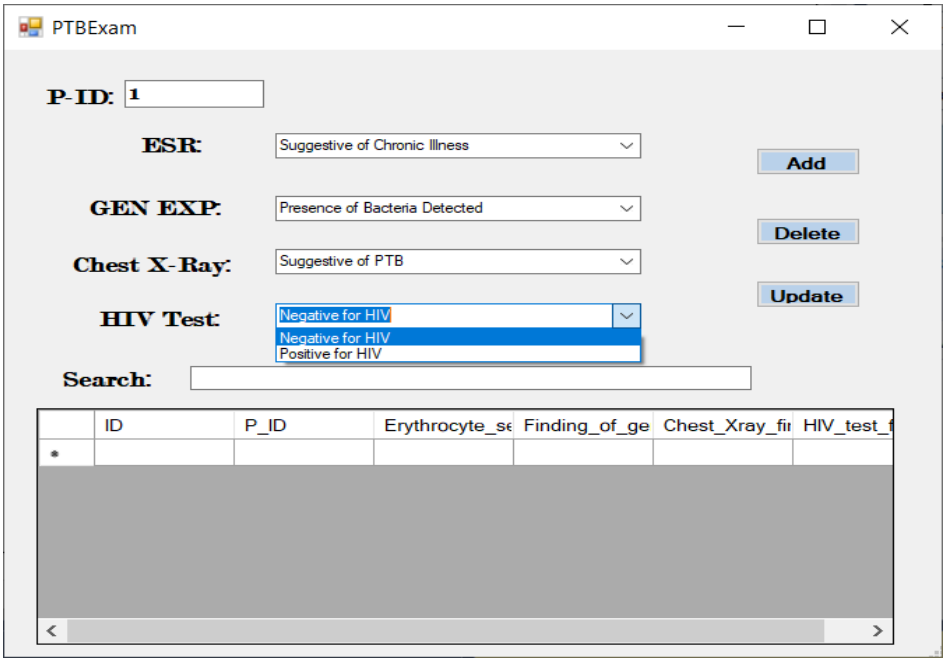
Once the symptoms are saved with respect to the patient's identification number, diagnosis will be performed to see the suspicion level of having TB, Pneumonia, Asthma or COPD. Next, user will run diagnosis for suspicion level greater than or equal to 5.0. By inserting patient ID, the laboratory technician or the radiographer will see the examinations order and after result is obtained, they will feed the results to the system on the specific patient identification number as shown in **Step 3**.

One of the examinations for PTB that is performed by the system, which is the chest X-ray image classification, will be performed. After the radiographer has taken a patient's chest X-ray image, he/she will save the image in a folder and open the system's chest X-ray analyser and choose that image for the system to classify. The system will then process and predict whether the image is normal or abnormal (indication of PTB) by also showing the chest X-ray for user as shown in **Step 3.1**.

- **Step 3.1: System's chest X-ray prediction**

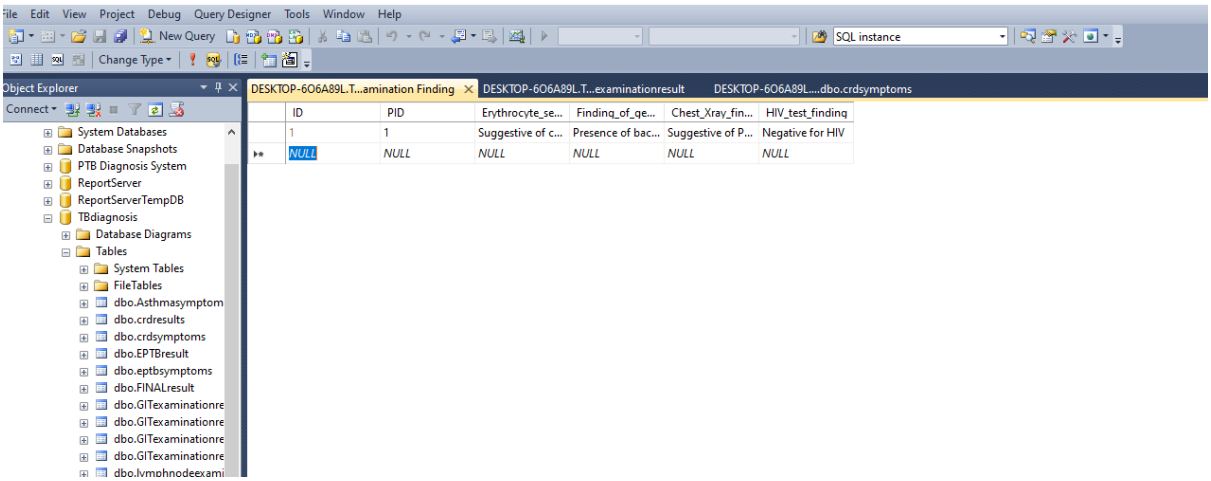


- **Step 4: Interface where user feeds laboratory and radiology findings**



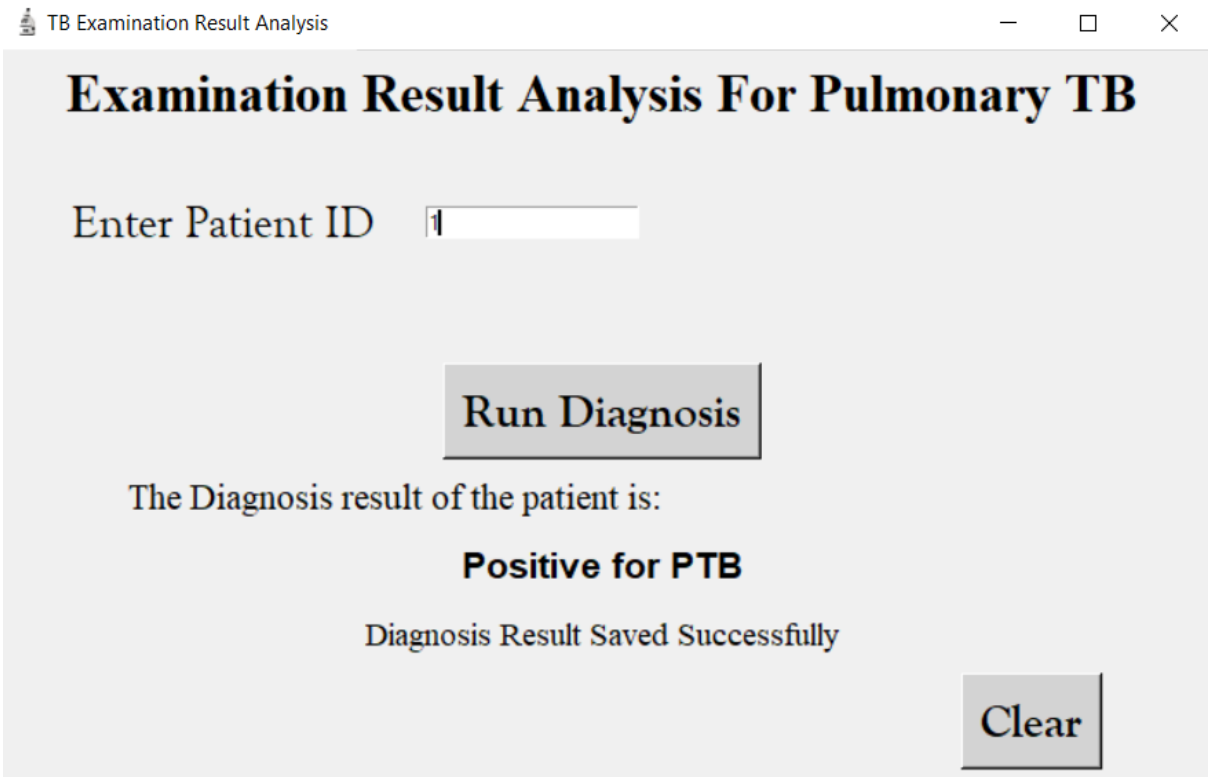
Once the examination results are found, the laboratory technician will enter and save the results on the database as shown in **Step 4**.

- **Database where patient laboratory and radiologic results are saved**

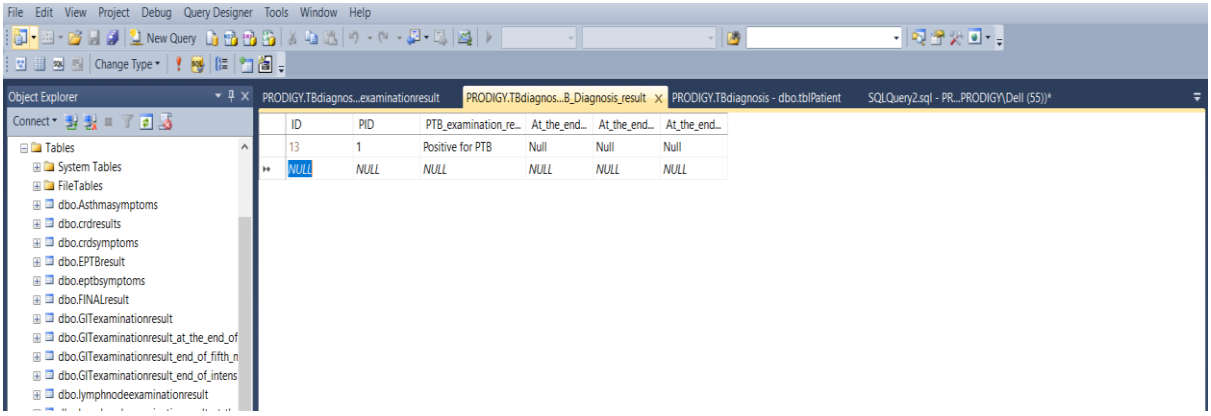


Finally, to analyse the examination findings and find the final diagnosis result, user will run examination result analysis using patient's identification number. The system will do the analysis and display the final diagnosis result and save it on the database as shown in **Step 5**.

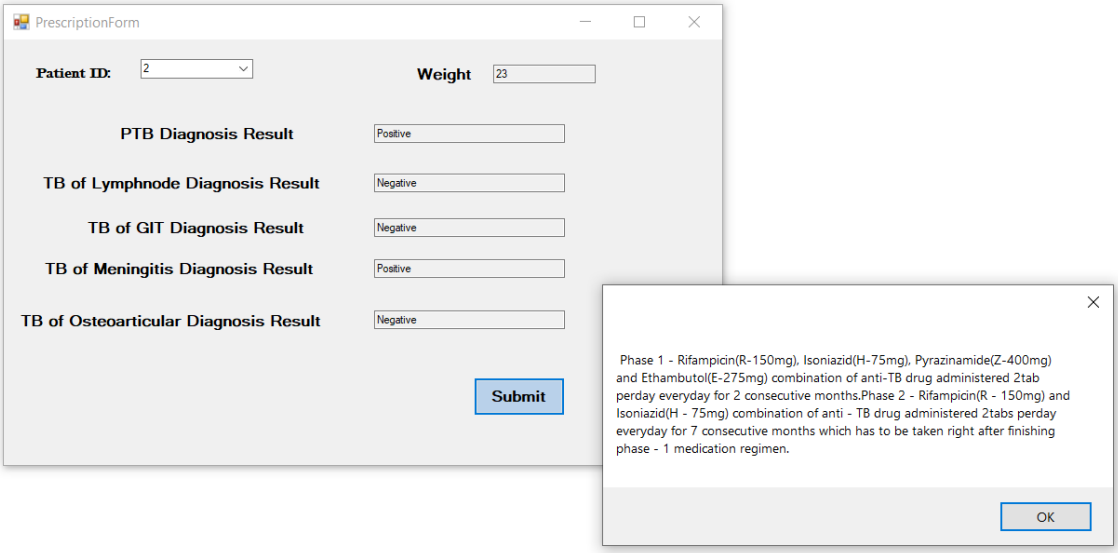
- **Step 5: Analysis of examination findings to obtain final result**



- **Final diagnosis result of patient saved in the database**



- **Step 6: Final report from all the diagnosis performed and medication prescription**



Once the diagnosis is done, the user will insert patient's ID to get the medication prescription for the diagnosis. System will display all the result from the examinations and display medication for the patient's diagnosis finding as shown in **Step 6**.