A web enabled fuzzy rule-based decision support system for dose adjustments of Duodopa infusion to patients with advanced Parkinson's disease

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Abstract

The main purpose of this thesis work was to develop a web enabled decision support system (DSS) based on a fuzzy logic inference system (FIS) to provide assistance in dose alteration of Duodopa infusion in patients with advanced Parkinson's disease, given data from motor state assessments and dosage. One data set was used for tuning the FIS and another data set was used for evaluating performance compared with actual given dose. Further, a web application with an interactive graphical user interface that presented alerts indicating non optimal dosage, dose summary information, advice for new dosage and options to calculate initial dose and evaluation of the DSS was implemented. Goodness-of-fit for the new patients (Observation data) was 65% for ongoing patients (Duodopa Infusion - Randomized Efficacy and Quality of life Trial study data) it was 98%. From the result of the system evaluation, it was found that the DSS could achieve expert's knowledge on an average 81% accurately. User evaluation, i.e. assessment of the DSS that it does the right thing right, an important step is needed to be done before implementing the DSS. The system incorporated the human knowledge to make a decision; it could work as an assistant of the clinical staffs in advanced Parkinson's disease.

Contents

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1 Introduction

Parkinson is a slowly progressive neurological disease. It affects a miniature area of cells in the mid brain. Gradual degeneration of these cells reduces a vital chemical called “dopamine”. This can fabricate one or more of the classic signs of PD such as stiffness, tremor and pain. Parkinson disease affects about 1% of all persons over the age of 60 and 15% of the patients were diagnosed before age 50. [1] There are four million people with Parkinson’s disease worldwide according to the estimates of the World Health Organization (11 April 2004 - 7th World Parkinson’s Day).

Ordinary treatment at the initial stage of this disease is ‘artificial dopamine’ (levodopa) in tablet form. Treatment of PD with levodopa was begun in 1960. [2] Levodopa is the main medicine used to treat Parkinson's disease. Medication must be individually tuned since too high dose leads to problems with uncontrolled movements. So adjusting their dopamine levels in order to function smoothly in their daily life is a problem.

For the PD patient it is very important to tune levodopa doses quickly to adjust their dopamine levels. Fluctuating plasma concentrations of levodopa become increasingly linked to variability in motor response with advanced PD. Motor fluctuations and dyskinesias are at least partially related to variations in blood levodopa concentrations, so fluctuation can be reduced by keeping levodopa plasma concentrations constant [21][22]. Significantly lower variability in plasma levodopa levels can be achieved with infusion of the stabilized carbidopa/levodopa (Duodopa) suspension compared with oral sustained-release tablets. [3]

Dosage of Duodopa was individualized for each patient’s needs. Therefore, no general schedules were available. Dosage of Duodopa was initially calculated from the daily dose of oral levodopa and then optimized. Morning bolus dose was large enough so that patient can reach a steady-state concentration and the infusion rate was adjusted to maintain this concentration level. Optimization of dosage depends on patient’s condition of the state where persistent Parkinsonian symptoms indicated that the dose was too low and persistent dyskinesia indicated that the dose was too high.

It is very important to design of systems to support individual decision making for this dose optimization tasks. A decision support system (DSS) can be any system that helps decision makers to make the decisions. A decision support system in health care is any computer program that designed to help health professionals to make clinical decisions. [4]. Decision support system supports, rather than replaces, human decision makers. Since 1960’s decision support systems have been developed for interpreting of findings and result in patient care, selecting of treatments, management of data and information, control of work-flow and monitoring of patient care processes and their outcomes.[5] Development of DSS beginning with building model-oriented DSS in the late 1960s and implementation of Web-based DSS in the mid-1990s. [6]

1.1 Project Background

This thesis work was a part of a project, IDOL (Intelligent Dudopa On-Line) in collaboration between Högskolan Dalarna, Uppsala Universty, NeoPharma Production AB and Clinitrac AB co-funded by KK-Stiftelsen. The background of the project was the need to individually tune dosage of medication for patients with advanced Parkinson's disease. On-line decision support for duodenal administration of levodopa to patients with Parkinson's disease based on wireless patient diary data assessments. Patients will necessitate fine adjustments of their dopamine levels to function in daily life. If the levels are low they will be stiff, shaking and in pain and if the levels are high they have problems controlling body movements. Since PD is a progressive disease, best medication dosage will be different over time. The purpose of the project is to develop a decision support system that recommends individual pump-settings based on the previous settings, the patient diary assessments and the number of booster doses requested by the patient. A web application was also to include for clinical staff as well as a user interface. [7]

1.2 Fuzzy Rule Based Decision Support System

Use of fuzzy logic in medical informatics has begun in the early 1970s. Fuzzy set theory, which was developed by Zadeh (1965), makes it possible to define inexact medical entities as fuzzy sets. It provides an excellent approach for approximating medical text [8]. Fuzzy models have some transparency; their information is interpretable, so as to permit a deeper understanding of the system under study. Now days it is also progressively more used in decision support system for the reason that it offers numerous advantages over additional conventional decision-making techniques [9]. A decision support system means a system that aids in generated decisions and involves goals and constraints that need to be met. System could be called a fuzzy rule based decision support system if the criteria involved were fuzzy in nature and depend on rules. [10] Fuzzy set theory and fuzzy logic are a highly suitable and applicable basis for developing rule-based systems in medicine and it proved to be a powerful tool for decision-making systems. [11] For developing decision support system in Parkinson's disease fuzzy set theory and fuzzy logic are a highly suitable and applicable for real-time monitoring of patient data. [12] An application of fuzzy logic for the development of a decision support system to model the prognosis of a patient suffering hearth failure treated with beta-blockers, showed how the basic rules, based on expert experience, are represented in a system based on fuzzy logic. [13]

1.3 Aim and Objective

The aim of this project was to build an assistant of the clinical staff that recommends individual pump-settings based on the previous settings, state assessments and the number of booster doses in order to adjust doses of duodenal levodopa infusion in advanced Parkinson's

disease. Patients will require fine adjustments of their dopamine levels to function in daily life. So it is very important to adjust levodopa doses (morning does, extra dose and flow rate) quickly.

1.4 Methodology

A decision support system using artificial intelligence-approach was developed that recommended individual pump-settings for optimizing individuals Duodopa dosage. Fuzzy rule–based system was used for implementing expert's knowledge with the help of mamdani fuzzy inference system. DSS system was constructed as three-tier architecture and for design /development object oriented concept was used. A set of observation data used for designing /developing the DSS and tested it using the data from DireQt (Duodopa® infusion - Randomised Efficacy and Quality of life Trial) study to see how it behaved.

In order to verify the system goodness-of-fit was calculated to see how it behaved compared to the expert's knowledge. Also mean difference and absolute mean difference was calculated to check the performance.

2 Materials

Data were found in two different formats and from two different clinical studies. One was observations of the new coming patients that were used for analysis, design, development and tuning for the parameters of fuzzy member ship functions of the decision support system (DSS). Other was DireQt study data for ongoing patient that was used for testing the DSS. Both data sets were used individually and together in order to system evaluation and performance measuring.

2.1 Data Description

Observation data were provided by NeoPharma AB, Uppsala, Sweden. Data consisted of dosage and status information from new Duodopa patients and were collected from April, 2002 to October, 2004 and there were 16 patients, observed between one and six consecutive days. Primary data were entered as a hard copy on a paper format where patient doses and states were taken through two or more days with patient code, and date. State conditions were defined by clinical examination of motor function of a standardized sequence of motor tasks: finger tips, altering hand movements, rising from a chair and walking. Global state was noted on a scale from -3/4 to +3/4 where negative values represented Parkinson symptoms due to too little medicine and positive values represented side effects due to too much medicine. This global treatment response scale, TRS, was graded from -3 (marked bradykinesia) to 0 (normal) and the dyskinesias scale was graded from 0 (normal) to 3 (severe choreic dyskinesia) [14]. Patients on treatment with Duodopa® used a portable pump for intraduodenal (into the gut) delivery of Duodopa. Doses were entered in attributes: morning dose, flow rate and extra dose. State and all doses information were entered over time from 6:00 to 23:00 hours. Infusion was not to be used at night. Dosage of Duodpa was individualized for each patient's need. Extra doses (0.1 -2 ml) could be delivered via the CADD-Legacy Duodopa pump. Starting and stopping of the pump, bolus doses (1 to 10 ml), extra doses, and infusion rates (1.3 to 9.8 ml/hr) were recorded.

DireQt data were taken from the DireQt (Duodopa® infusion - Randomised Efficacy and Quality of life Trial) study. This study was a three + three weeks crossover study of Duodopa vs. conventional anti-Parkinson medications with blinded assessment of Parkinsonism and dyskinesias from video recordings of patients and using the TRS. Patients were video recorded every 30 minutes from 9:00 to 17:00. Main objective of this study was to compare continuous intraduodenal infusion of Duodopa as monotherapy to treatment with any antiparkinsonian combination therapy in patients with advanced idiopathic levodopa-responsive PD, suffering from motor fluctuation in spite of individually optimized treatment [14]. Only the days when the patients were on Duodopa was used as test data.

2.2 Environment

For the data analysis, cleaning, filtering and normalization Microsoft Offices Excel for windows XP was used. The relational database management system (RDBMS) MySQL was used for defining constrains and storing data as different objects with proper relations.[15] To connect MySQL with a web application and the DSS, MyODBC-3.51.06 was used.[16]

For object, class design and database design Microsoft Office Access for windows XP and Rational Rose 98 Enterprise version was used.

For Fuzzy Inference System, NRC FuzzyJ Toolkit [17], a Java(tm) API for representing and manipulating fuzzy information, created at the National Research Council of Canada (NRC), was used. The toolkit consists of a set of classes (nrc.fuzzy.*) that allows a user to build fuzzy systems in Java. The IDE (Integrated Development Environment) used here was JBuilder 2005 Foundation; a software from Borland Software Corporation.

For the web application, Cold Fusion MX 7 server developer edition, java script, HTML and Cold Fusion Markup Language (CFML) were used. [18]

On the above tools, all were in free of cost except Cold Fusion, but there were some reasons for using it. The most common reason for a web developer was that Cold Fusion has built in tags and fully tag based language. It can support custom tags and has capability to interact with external components and other scripting language. Summing up the power of Cold Fusion was found in the April 2000 issue of SQL Server Magazine - with rate each of the 3 offerings where 1 being the best in that category and 3 being the worst. [19]

Table 1: Compare chart [19]

Environment	Ease of Use/HTML Integration	Support for Databases	Cross-Platform Support	Upfront Costs	Extended Costs
ASP	2	1	3	2	2
JSP/Servlets	3	3	1	1	3
Cold Fusion	1	2	2	3	1

From the table no 1, can compare the 3 and find the reason why Cold Fusion was chosen for the web development. The main advantage it gives is the time for developing sophisticated and useful applications with it is little and it is the less expensive to maintain for a serious web site.

For my self, I had one year experience on clod fusion for developing a garments portal “http://www.bangladeshgarments.info/” for my home country in a local software company.

3 Methods

For developing a decision support system in order to adjust Duodopa doses in advanced PD, an artificial intelligence approach using a fuzzy logic rule based system was used. The steps used to build the decision support system are outlined in the figure no 1:

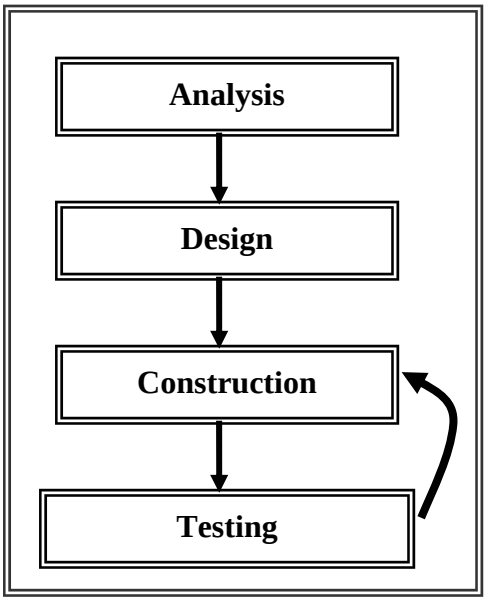


Figure 1: Steps for developing the decision support system

Analysis: Analysis was the first phase of the development that involved acquiring a general understanding of the problem. The process involved extracting knowledge from data. Acquiring and formalizing expert knowledge was a very important task. Information was gathered and found as a hard copy with patient name, date, state condition and amount of doses over time for the objective of constructing data model. After data analysis, data accumulated and a relational database management system was used to store and normalize the data. Business logic and rules for fuzzy inference system (FIS) were also defied in this phase by the help of observations data and expert knowledge.

Design: System was designed in *design* phase using three tires architecture: front-end was the user interface (web-application), middle-end was DSS and the back-end was the database. All business logic, fuzzy technique, fuzzy inference system and calculation were implementing in the middle-end. A block diagram for architecture of the decision support system is shows in figure no 2.

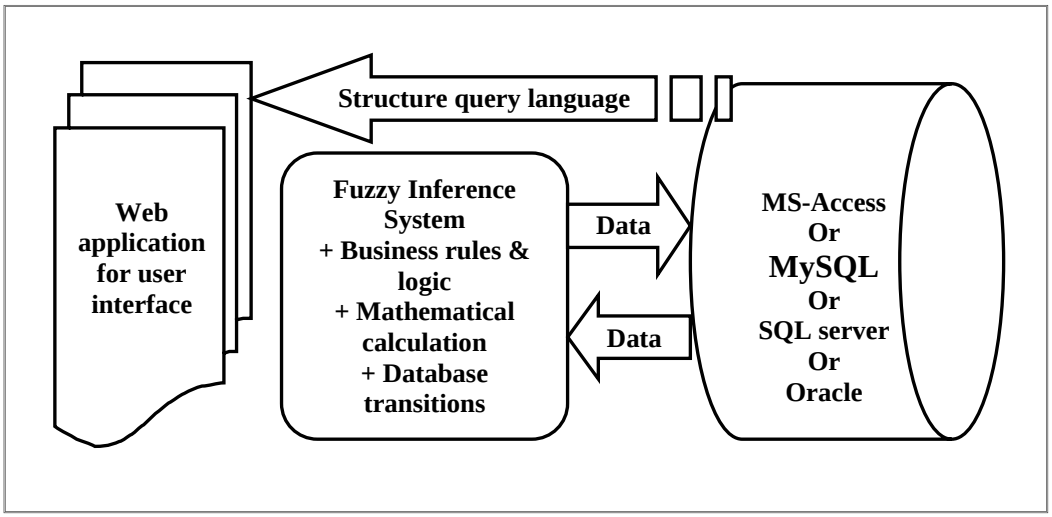


Figure 2: Architecture of the system

Back-end: A relational database named "DSS" was built that connected with the decision support system to feed data as an input and also to store advised doses and summarized doses information which were used in web application.

Middle-tier: All business logic, fuzzy inference system, implemented rules, mathematical calculation and database transition were done in middle layer. The figure no 3 illustrates how old doses and state of patient from database were used to feed as input to the DSS, that generated a summary of doses information and alerts for doses in various situations, recommended new dose adjustments by using the fuzzy inference system and evaluated the difference between advised doses and taken doses.

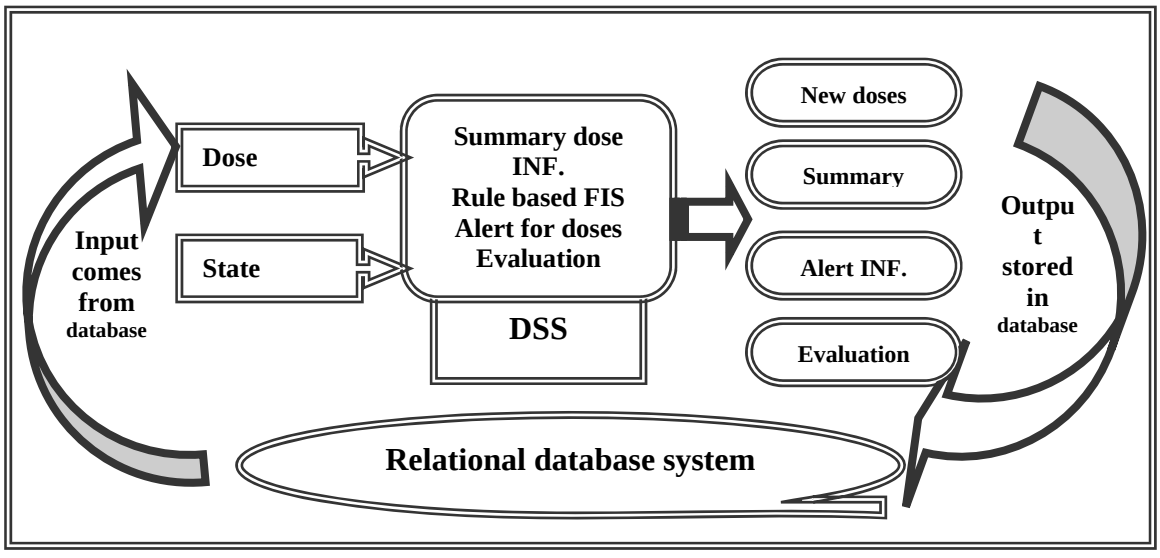


Figure 3: Architecture of the decision support system

Front-end/user interface: This was the web application that should be used by the hospital staff. An applet was included in the web application for calculating initial doses for new patients. In order to check period wise patient dose summary information, three web pages were included. Alerts for patient's doses were shown; users could search by date, patient

name, patient id and alert option wise. New dose recommendation with suitable reason was shown where users could search by date, advised option and patient wise.

Construction: For constructing database and initial data in *construction phase*, a database script was generated to make it easy to use for both the developer and the end user.

Business level was created with the help of object oriented programming where information were divided in various objects, such as database object, fuzzy rules object, calculation object and so on. All objects were implemented as a class with relationship and data were handled by using public, private modifiers.

To get summary doses information, maximum, minimum, mean and standard deviation value were calculated for each patient in each day's observations with different categories; such as number of extra doses, total dose, start time, end time, so on.

In the fuzzy inference system for calculating new doses, all values of doses and state conditions were treated as fuzzy variables that were described by a fuzzy set. A fuzzy set was identified by its linguistic value and it was necessary to evaluate the membership value (MV) of an element to the fuzzy set. Membership functions of those fuzzy sets were represented by the degree of membership in the range from 0 to 1. Fuzzy systems contain rules, based on domain expert's experience that was found in analysis phase, and implemented here to carry out evaluations. Every variable were represented by a fuzzy set (FS) and "fuzzyfied" using appropriate functions. When data were feed the system, predefined rules were fired and the corresponding consequences were shown, with a likelihood indicator. "Defuzzyfied" values that came out after firing rules were the new advised doses and stored into database.

Testing: The system was tested and evaluated in the *testing phase.* Test data was taken from a clinical study in text file format. Then data were cleaned, filtered and made ready for test. System generated error difference and evaluation could be checked by using different options --patient wise, date or using dose option. To get less error for observations data the parameters of membership function in fuzzy inference system was tuned.

3.1 Analysis

Design data were found as a hard copy format and it was very important to extract knowledge and compare with the expert knowledge because depending on data, rules were defined and the system was designed and developed. In this part, the whole work was divided in to the following tasks:

1. Data analysis.
2. Define relations.
3. Define constraints.
4. Data entry.
5. Define business logic.
6. Define rules for FIS.

3.1.1 Data analysis

Data were taken by the doctors for each patient in one up to six days. In a graphical format, clinical had put patient's code, date, morning dose, flow rate, extra dose, state and time. Figure 4 shows a sample format.

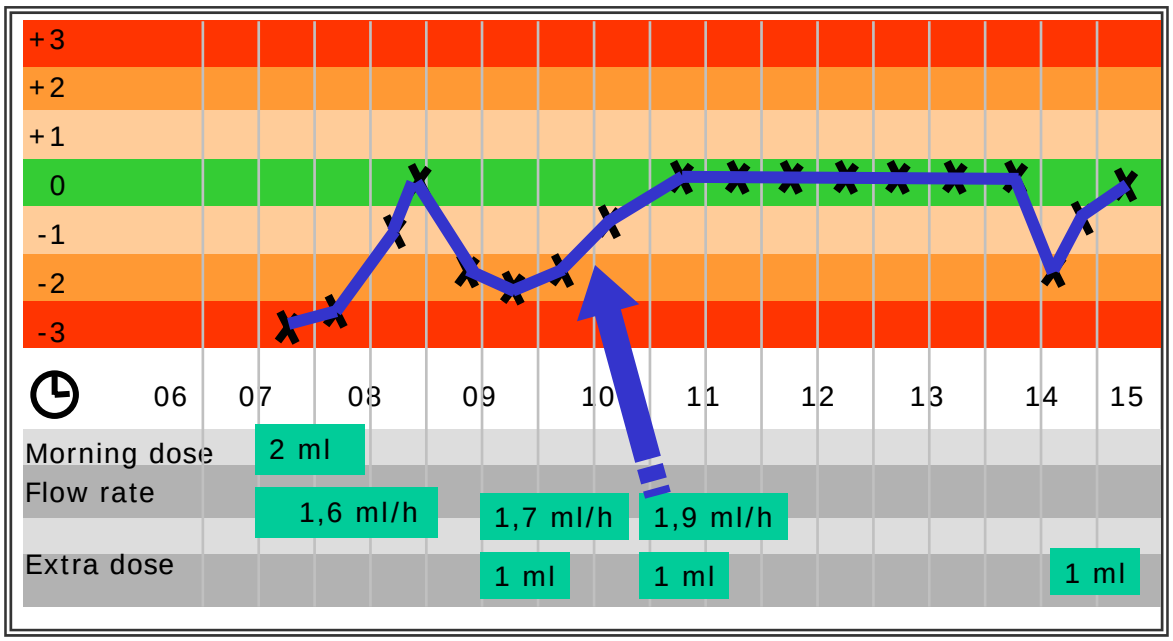


Figure 4: Raw data format for checking state in time of observation study [23]

States were defined from +3 to -3 but some patients had state from + 4 to – 4 in various times of day. A patient (sample figure no 4) were to start his/her treatment by taking a morning dose (2 ml at 7:15 a.m. and flow rate was 1.6 ml/h 7:45 a.m.) At that time, state was -3 but after few hours, at 8:30 a.m., it was 0 (normal). At 9:30 a.m. state was -2.5 so patient had taken one extra dose as 1 ml and also increased his/her flow rate by 0.1 ml/h. At 10:00 a.m. it was still in negative condition so patient had again taken one extra dose as 1 ml and also increased flow rate by 0.2 ml/h. Now at 11:30 a.m. to 13:45 a.m. state was in zero that means in the normal position. In general, morning dose and flow rate were started between 6 to 8 o'clock and state were checked in different time slots. Depending on the state condition, doctors gave extra dose and also changed the flow rate. Flow rate and extra dose were increased if and only if the state was in negative condition but morning dose was changed only for next day.

3.1.2 Define relation

After analysing the information and getting knowledge from experts, relational data objects with their attributes were found, such as patient information {patient id, patient name, state scale}, old doses information {doses id, date, dose time, morning dose, extra dose, flow rate, state}, new doses information {new dose id, date, dose option, dose time, old dose, state, state time, new dose, advise reason} and so on.

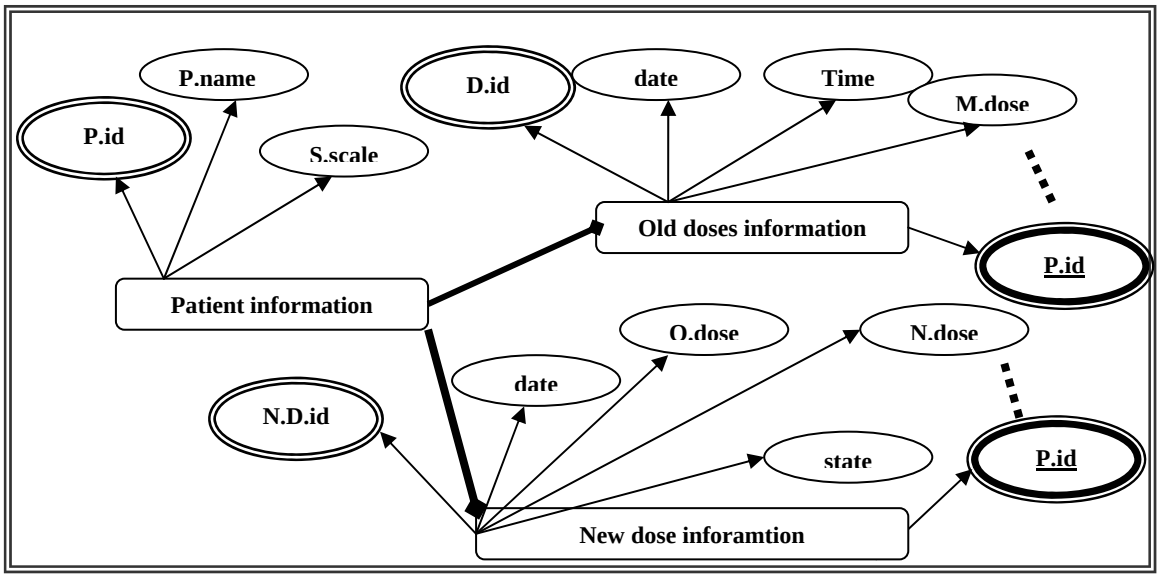


Figure 5: Sample for entity relationship model

In the figure 5, patient information was related to the old doses information and new dose information. One-to-many relationships were found and shown in this figure where P.id, D.id and N.D.id were primary keys of patient information, old doses information and new doses information; P.id was also a foreign key as a reference of patient information.

3.1.3 Define constraints

Constraints were defined in patient information's {patient id, patient name, age, state scale}, old doses information's {doses id, date, dose time, morning dose, extra dose, flow rate, state} and new doses information {new dose id, date, dose option, dose time, old dose, state, state time, new dose, advise reason}depending on data analysis and expert knowledge. They are defining in tables no 2, 3 and 4:

Table 2: Constrains for patient information

Patient's information				
Attributes	**Type**	**Size**	**Nullity**	**Duplicity**
patient_id (pk)	Integer	5	Not null	Not
patient_name	Varchar	255	Null	Yes
state_scal	Integer	1	Not null	yes

Table 3: Constrains for old doses information

Old doses information				
Attributes	**Type**	**Size**	**Nullity**	**Duplicity**
doses_id (pk)	Integer	5	Not null	Not
Date	Date	-	Not null	Yes
dose_time	Time	-	Not null	Yes
morning_dose	Float	(13,12)	Null	Yes
extra_does	Float	(13,12)	Null	Yes
flow_rate	Float	(13,12)	Not null	Yes
State	Float	(13,12)	Null	Yes

Table 4: Constrains for new doses information

New doses information				
Attributes	**Type**	**Size**	**Nullity**	**Duplicity**
new_doses_id (pk)	Integer	5	Not null	Not
date	Date	-	Not null	Yes
dose_option	Varchar	255	Not null	Yes
dose_time	Time	-	Not null	Yes
old_dose	Float	(13,12)	Not null	Yes
state	Float	(13,12)	Not null	Yes
state_time	Time	-	Not null	Yes
new_dose	Float	(13,12)	Not null	Yes
advice_reason	Varchar	255	Not null	Yes

3.1.4 Data entry

Data was entered into text files named tblPatient.txt for patient information and tblDose.txt for old doses information by tab separator which was used to load data in MySQL database. Sample data for patient information and old doses information are shows in the tables no 5 and 6:

Table 5: Patient information

Patient_ID	Patient_Name	S_Scale
1	Skj I	3
2	BQ	3
3	KB	3
4	Anita Soondra	3
5	Arbets	4
6	Ir	3
7	ÖB	3
8	Akers Hue	3
9	R.O	4
10	MP	4

Table 6: Old doses information

Date	Dose_Time	Morning_Dose	Extra_Dose	Flow_rate	state	Patient_ID
3/2/2004	7:00	5		4.2	-2.1	1
3/2/2004	7:45			4.2	-2.5	1
3/2/2004	9:00			4.2	1	1
3/2/2004	10:00			4.2	1	1
3/2/2004	11:30			4.2	1	1
3/2/2004	12:00			4.2	1	1
3/2/2004	13:30			4.2	0.7	1
3/2/2004	14:00			4.2	1.6	1
3/2/2004	15:00			4	1.9	1
3/2/2004	15:30			4	0.9	1
3/2/2004	16:00			4	1.9	1
3/2/2004	17:00			4	0	1
3/2/2004	18:00			4	-0.1	1
3/2/2004	19:00		1	4	0	1
3/2/2004	19:45			4	1	1
3/2/2004	21:00			4	-1	1
3/2/2004	21:30			4	-0.1	1
3/2/2004	22:00			4	-0.1	1
3/4/2004	7:00	5		4	-1.9	1
3/4/2004	8:00			4	0	1
3/4/2004	9:15			4	0.9	1
3/4/2004	10:30			4	0.5	1
3/4/2004	11:30			4	0.5	1
3/4/2004	12:30			4	0	1
3/4/2004	14:00			4	0.5	1
3/4/2004	15:00			3.8	0	1
3/4/2004	16:15			3.8	1	1
3/4/2004	17:45			3.8	0	1
3/4/2004	19:00			3.8	1	1
3/4/2004	20:00			3.8	1	1
3/4/2004	21:00			3.8	0.3	1

3.1.5 Define business logic

Depending on expert knowledge doses were handled into more than two different ways: first one was to calculate initial doses and another one was for doses adjustments. To handle those types of doses i.e. morning dose, flow rate and extra dose various logics were found. Depending on the patient taken doses different logics were defined for generating dose alert.

Initial doses calculation

For calculating initial doses for new patients, clinical staff should input total daily dose and first tablet dose in milligram, which should be less than total dose. The DSS should then calculate starting values for the morning dose, extra dose and flow rate. The business logic of initial doses calculation is defined below:

- Morning dose: Usually it was in milliliter which was 90% of first tablet but clinical staff might change the percentage.
- Flow rate: It was also in milliliter, dose per hour excluding first tablet form total dose in each day where total hour was 16 from 6:00 to 22:00.
- Extra dose: 20% of morning dose in milliliter.

Doses adjustment

Doses were adjusted by generating new doses that depended on state condition, so states were scanned in every 15 minutes interval for each day. From the expert's knowledge different logics were defined to adjust doses; they are as follows:

- Morning dose: It was generated at the end of the day as a new dose for the next day.
  - If patients had not taken any extra doses within one hour after morning dose, then state condition were considered.
  - State was considered from 45 minutes to 90 minutes after the dose in priority basis.
    - 60 minute was first priority.
    - 75 minute was 2nd priority.
    - 45 minute was 3rd priority.
    - 90 minute was last priority.
- Extra dose: Depending on state, new extra dose was generated, so every 15 minute interval states were scanned.
  - If patients had taken no extra doses within two hours after taking an extra dose then states were considered.
  - State was considered from 45 minutes to 90 minutes after the dose with same priority as morning dose that described above.
- Flow rate: New flow rate was generated every 4 hours and regression slope was calculated by plotting states against dose time.
  - If patients had not taken any extra doses or morning dose within four hours after changing last flow rate, then state and dose time were scanned.
  - If number of states were more than one within 4 hours interval then states and times were considered for calculation.
  - State could be rising and falling by the value of regression slope.

Doses alert

Alerts were generated depending on how much doses such as extra dose, flow rate and total dose were taken by the patient.

- Extra dose: If patients were taken extra doses more than three times then one alert need to be generated.
- Flow rate: If patient were changed their flow rate more than three times then an alert need to be generated.
- Total daily dose: If total amount of daily doses occur a difference (20%) from previous day then an alert need to be generated.

3.1.6 Define rules for FIS

Rules were defined for morning dose; extra dose and flow rate depending on old doses information and states that were based upon expert's knowledge.

- Morning dose: Two rules were defined depending on state condition for applying to the FIS
  - If state was negative then new morning dose was increased 20% from old dose.
  - If state was positive then new morning dose was decreased 20% from old dose.
- Extra dose: Two rules were defined depending on state condition for applying to the FIS
  - If state was negative then new extra dose was increased 20% from old dose.
  - If state was positive then new extra dose was decreased 20% from old dose.
- Flow rate: Two rules were defined depending on regression slope for applying to the FIS
  - If state was falling then new flow rate was increased 20% from old dose.
  - If state was rising then new flow rate was decreased 20% from old dose.

3.2 Design

The architecture of the DSS was designed in this phase. The DSS was implemented in 3-tier architecture. The layers were: bottom layer: database and middle layer: Fuzzy rule base system i.e. DSS and top layer: interface design i.e. web application. Designing task is dividing into the following parts:

1. Database design.
2. Design of the decision support system.
3. Design of the web application.

3.2.1 Database design

After data analysis and defining relation and constrains it was the time to design the database. From previous analysis, patient information, old dose information and new information were found, but it was necessary to add some more objects, such as summary information, alert information and evaluation information in order to store data and build the web application. So, the final designed database named “DSS” appears in the figure no 6:

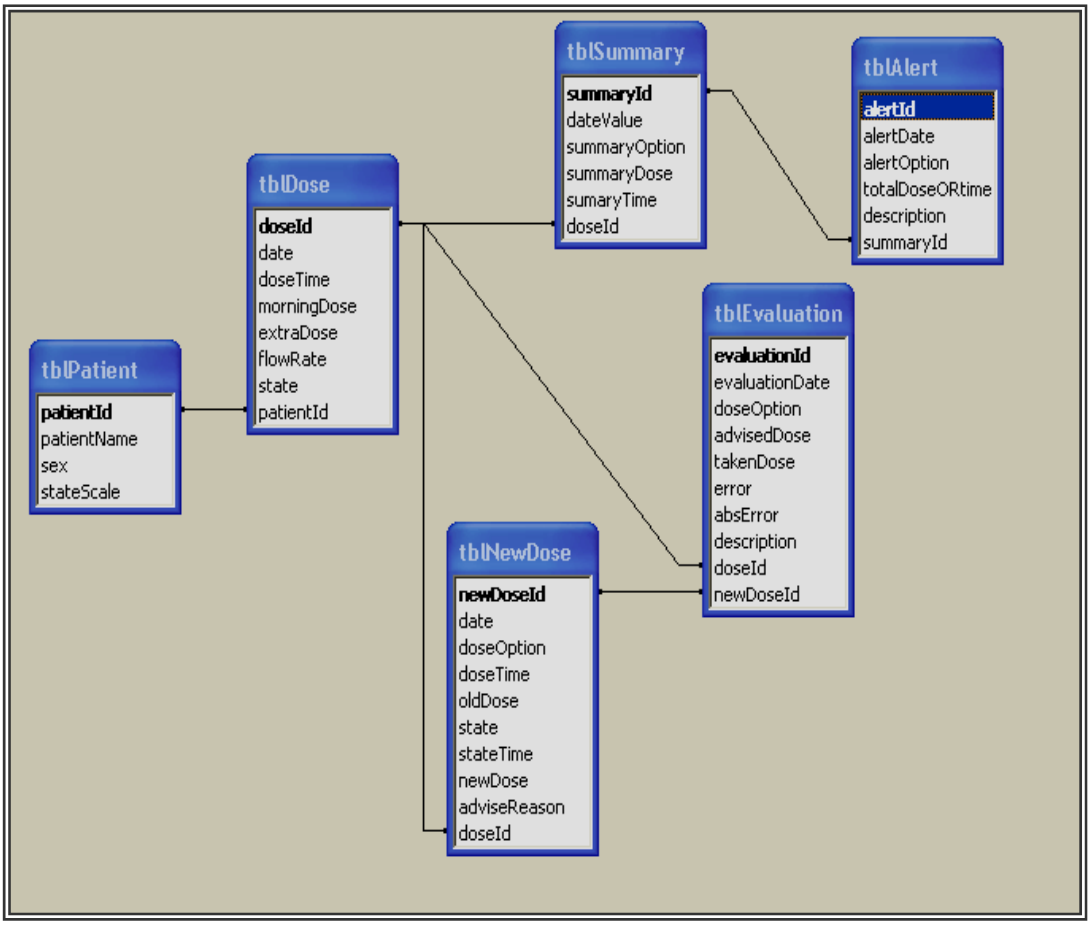


Figure 6: Relational database management system

In the figure 6, old dose information was related with new dose information, summary information and evaluation information by one-to-many relationships. Evaluation information was related to new dose information and old dose information by different attributes which showed many-to-many relationships. Other entities were related with each other by one-to-one relationships. All entities had primary key, null and foreign key constrains. This relational database was used for both decision support system and web application.

3.2.2 Design of the decision support system

The decision support system not only generated new doses information but also generated summary information, alerts for unusual doses and evaluation between the new and old doses. The main part of the DSS was the fuzzy inference system that generated new doses, so different objects and classes were used for development. The design task is breaking down as follows:

1. Class design.
2. Design fuzzy inference system.

Class Design

All objects were treated as package those had some classes and sub classes. Each class had its won individual properties and functionality. Properties and functions were public and/or private. All classes were public and related with each other by association, aggregation, generalization and dependency. The class design diagram is shows in figure 8:

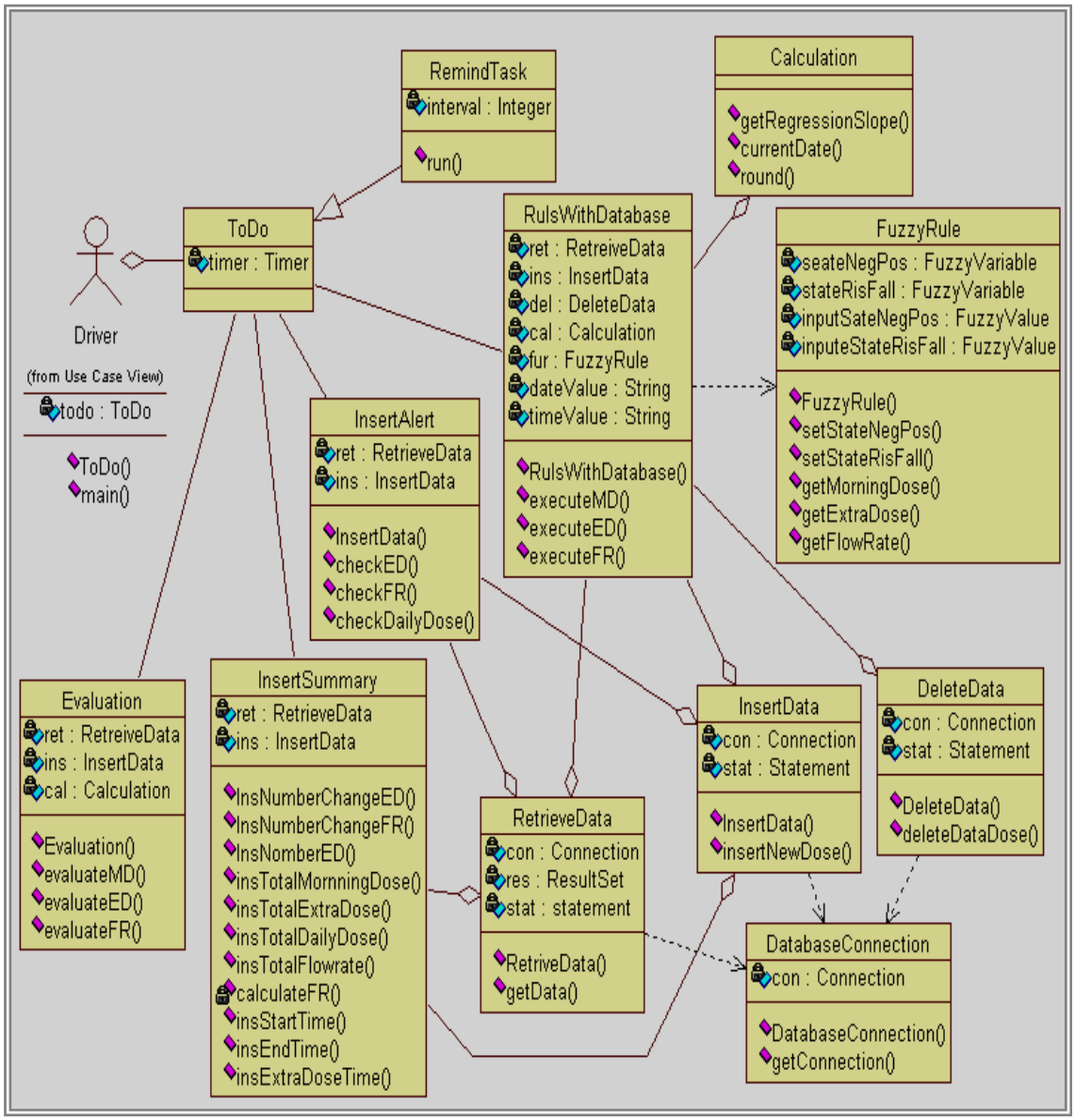


Figure 7: Class diagram of DSS

In the figure no 8, “ToDo” and “RemindTask” classes were related to each other by generalization. “RetrieveData”, “InsertData” and “DeleteData” classes were depended on the “DatabaseConnection” class. The”ToDo” class was associated with the “RulesWithDatabase”, “InsertAlert”, “InserSummary” and “Evaluation” classes. The class “InserAlert” was aggregated with “RetrieveData” and “InsertData” classes. ”Driver” class had a main method where it called the “ToDo” class as instance and “ToDo” class had a time schedule that handled summary, alert, fuzzy and evaluation classes. The “RulesWithDatabase” class had all business logic about how clinical staffs had given doses to the patients and the fuzzy inference system generated new dose for patient dose adjustment with the help of the “FuzzyRule”class. The “Calculation” class calculated necessary tasks such as regression slope, current date time e.t.c. “InsertAlert” generated alert with help alert’s business logic. “InsertSummary” class calculated summary and stored those to the database by the help of “RetrieveData” and “InsertData” classes. “RetrieveData”, “InsertData” and

"DeleteData" classes handled database transaction with help of "DatabaseConnection" class that contained a function to handle database connectivity.

Design fuzzy inference system

A fuzzy logic technique was used to design an inference system (FIS) using The Mamdani fuzzy inference. The basic structure of fuzzy logic expert systems, commonly known as fuzzy inference system (FIS), is a rule-based or knowledge-based system consisting of three conceptual components: a rule base that consists of a collection of fuzzy IF–THEN rules; a database that defines the membership functions (MF) used in the fuzzy rules; and a reasoning mechanism that combines these rules into a mapping routine from the inputs to the outputs of the system, to derive a reasonable output conclusion.

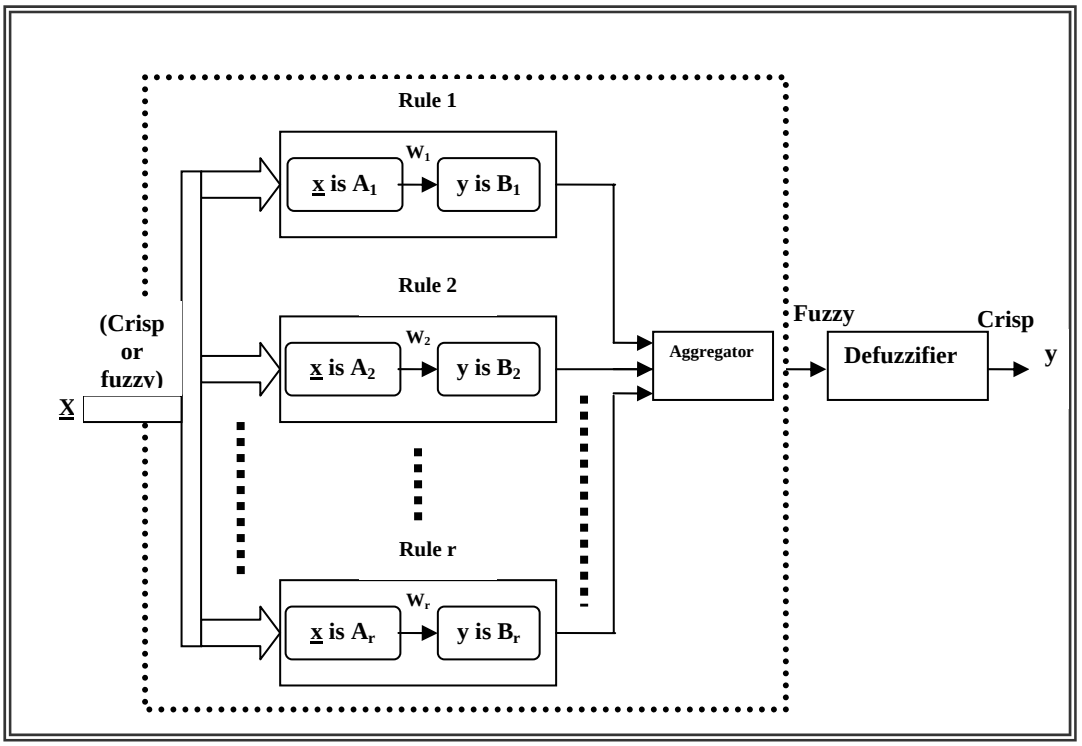


Figure 8: Block diagram of fuzzy inference system [11]

In the figure no 9, the dashed line indicates a basic fuzzy inference with fuzzy output and the defuzzification block serves the purpose of transforming an output fuzzy set into crisp single value. A basic FIS can take either fuzzy input or crisp inputs, but the outputs it produces are almost always fuzzy sets. It is necessary to have a crisp output then a method of defuzzification to extract a crisp value that best represents a fuzzy set and fuzzy inference system is used as a controller. [11]

In this decision support system, fuzzy inferences system was designed for morning dose, extra dose and flow rate. The designed figure for FIS is shows in figure no 9:

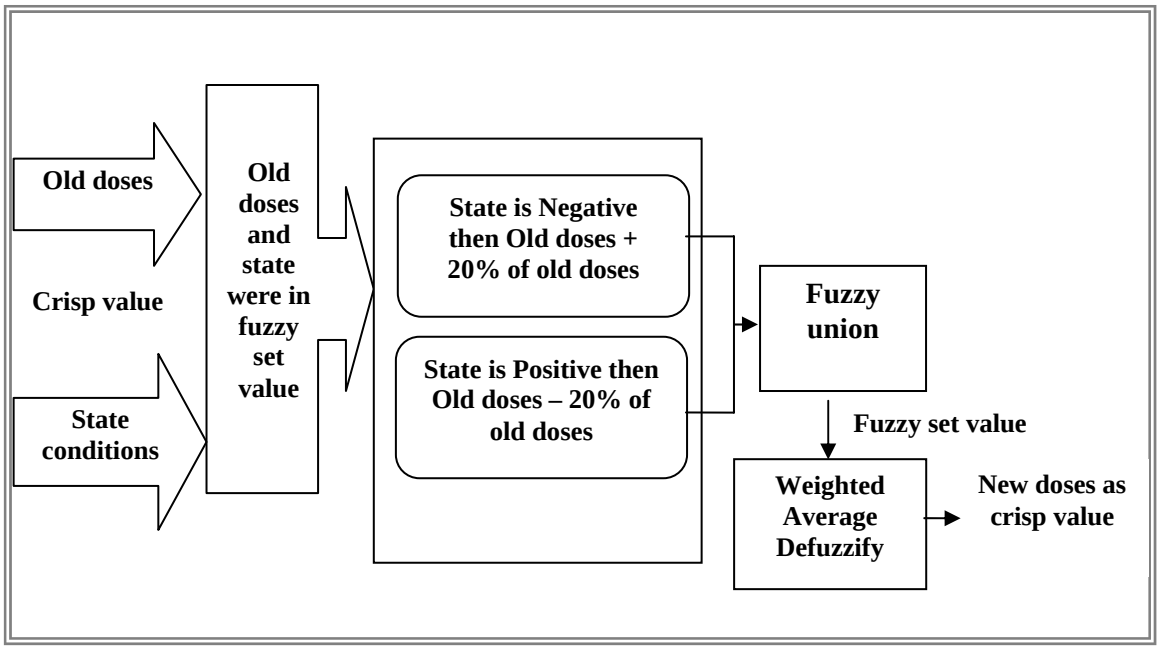


Figure 9: Fuzzy inference system for DSS

In the figure no 10, old doses and state conditions that come from the database as a crisp values, were converted to fuzzy set values by the fuzzy inference system. Output comes as fuzzy set value which were aggregated by fuzzy union and finally new doses were found as a crisp value that was done by weighted average defuzzify.

3.2.3 Design web application

Web application was needed to present patient's information for the clinical staff in pages. Web pages contained various search options to facilitate clinical staff searching and browsing for proper information. Different search options and various charts given in the web application are described here:

1. *Search option:*

- Period wise search: Treatment taken by the patients for a period. Clinical staffs could enter "From date" and "To date" in the search page to see summary of dose information for a period. Resulting information can be shown in another page.

- Patient wise search: Many patients were taken their treatment in one day. It was necessary to see all patient doses information for each day.

- Date wise: Patients were taken treatment in many days (more than one day). So individual patient doses information needed to present and facilitated for search.

- Dose option wise: Three doses option information were found such as morning dose, extra dose and flow rate. So dose option wise information needed to present in the page.

2. *Different charts*

- State condition: State were plotted against time value as a bar diagram for each patient in different dates.

- Doses value: All doses were plotted against time value as a bar diagram for each patient in different dates.

- Comparison: New dose values and old dose values were plotted against time for each patient with different dose options in different dates.

- Comparison: Advised and taken dose values were plotted for all patients, dose options and individual patients, dose options wise

- Mean comparison: Average advised and taken doses values were plotted against different doses options for each patient in different dates.

3.3 Construction

Construction was started from database, MySQL by generating a sql script. Script was written with standard query language in a .sql file format named database.sql. Data were loaded from .txt file name tblPatient.txt and tblDose.txt. ODBC connection was used with data source name which was used to make connection for DSS and web application. DSS was constructed in java with different classes and functions. All classes were under its won packages and all packages were under a project named DSS. A driver class was used to handled others sub classes. For web application Cold Fusion Markup Language was used for database query, if then else logic, function and for representing data. HTML language was used for creating tables, text box and so on. A Java script was also used for navigating pages.

3.3.1 Business logic

In DSS, business logics were implemented for three dose categories morning dose, extra dose, flow rate and dose alerts.

Morning Dose

Morning dose was taken by the patient one time per day, decision were advised at the end of the day for the morning dose of next day. State conditions were considered if and only if the patients didn't take any extra dose within two hours after taking their morning dose. New dose size was advised in priority basis (60, 75, 45, 90 minutes) after taking morning dose. Flow chart for morning dose is defined in figure 11:

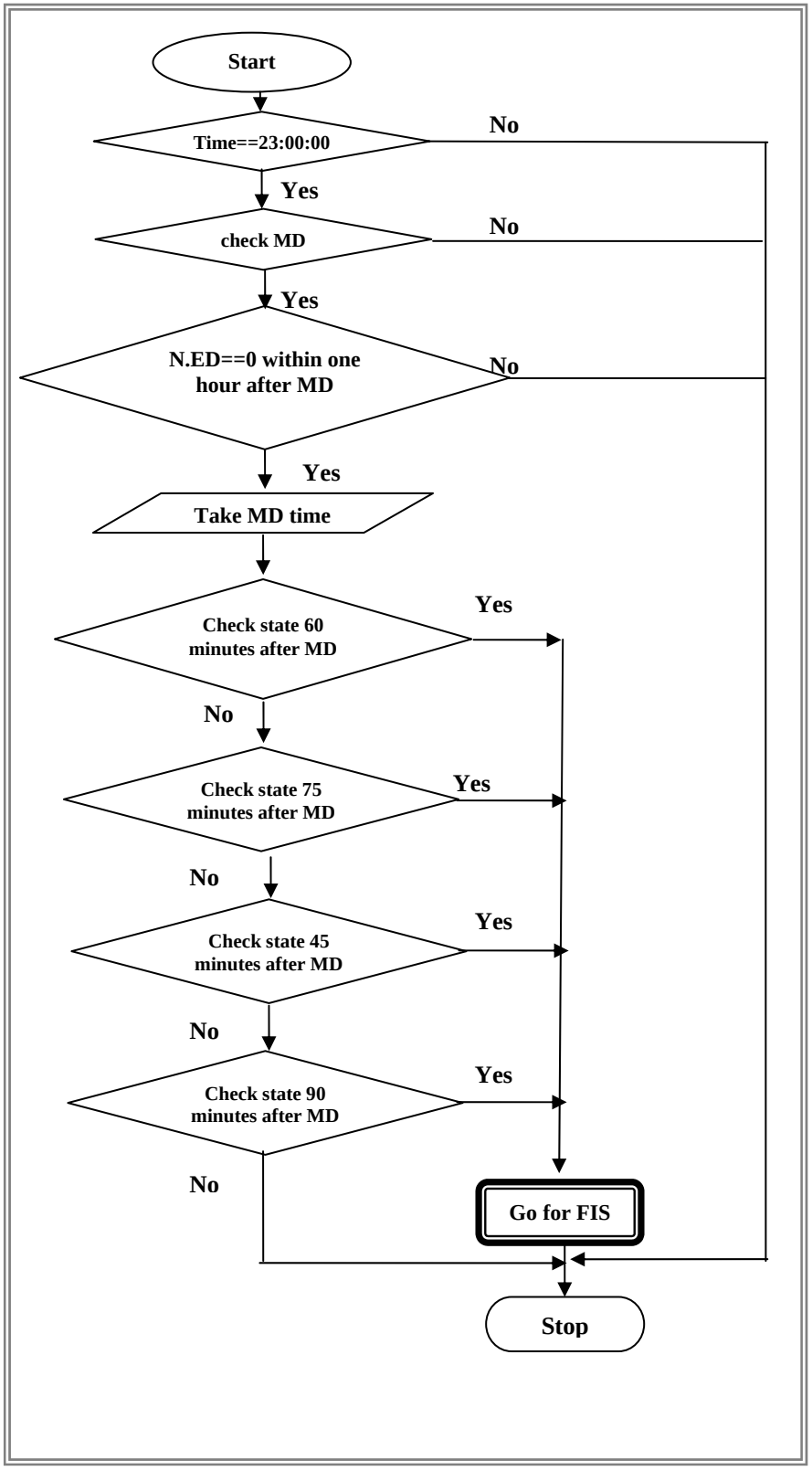


Figure 10: Flow chart for morning dose.

Extra Dose

Patients were taken some over doses which was called extra dose that depend on state condition. State was scanned from database in 15 minutes time interval but states were considered if patients didn't take more than two extra doses within two hour after taking first extra dose. New extra dose size was advised in same priority as morning dose. The flow chart is in figure no 12:

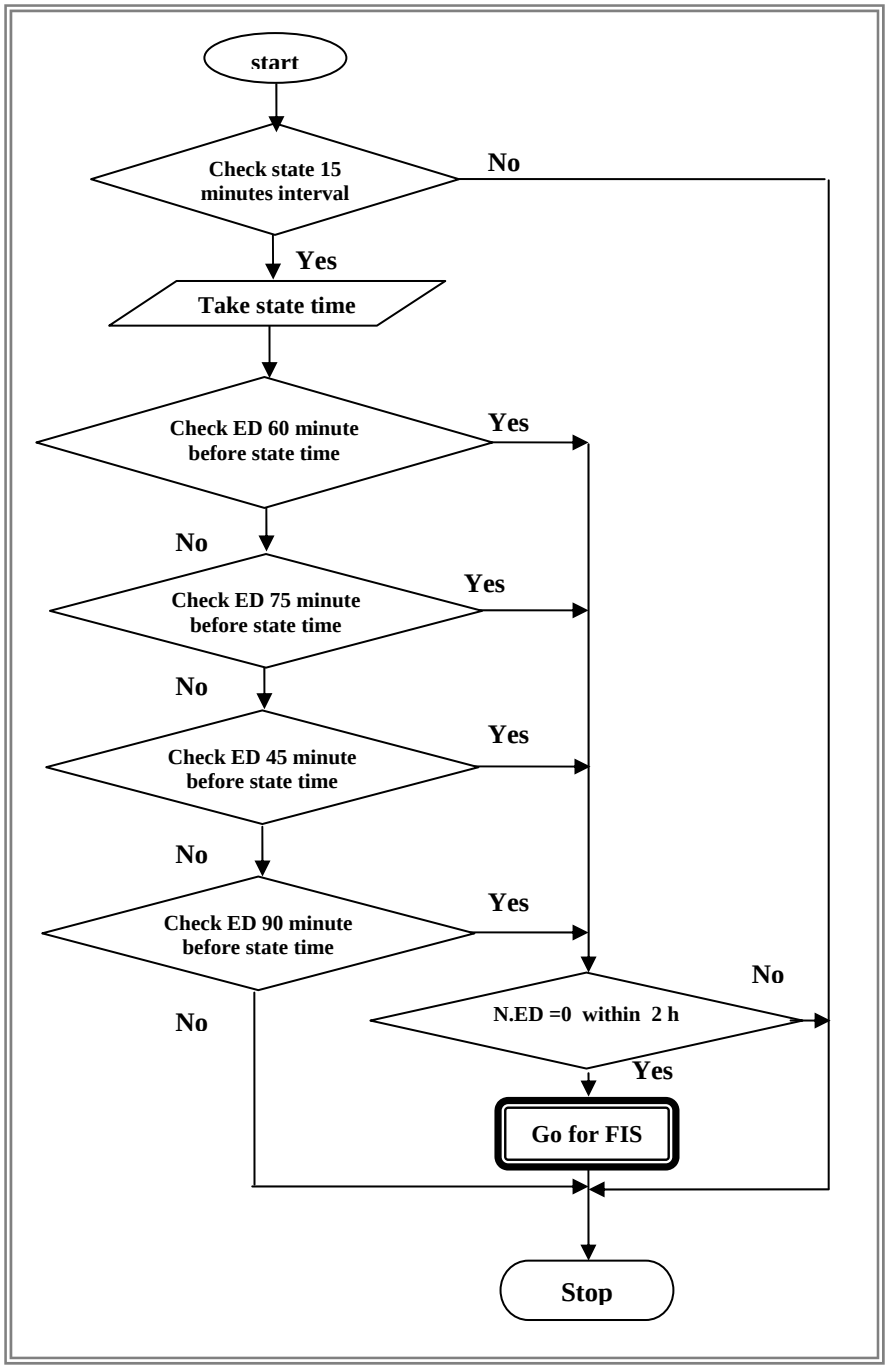


Figure 11: Flow chart for extra dose

Flow rate

New flow rate size was advised in every 4 hours interval, within four hours if patients didn't take any extra dose and morning dose then state condition and dose time was considered for calculating regression slop. Slop value could be negative, positive and normal that defined state condition rising, falling and normal. Flow chart for flow rate is given figure 13:

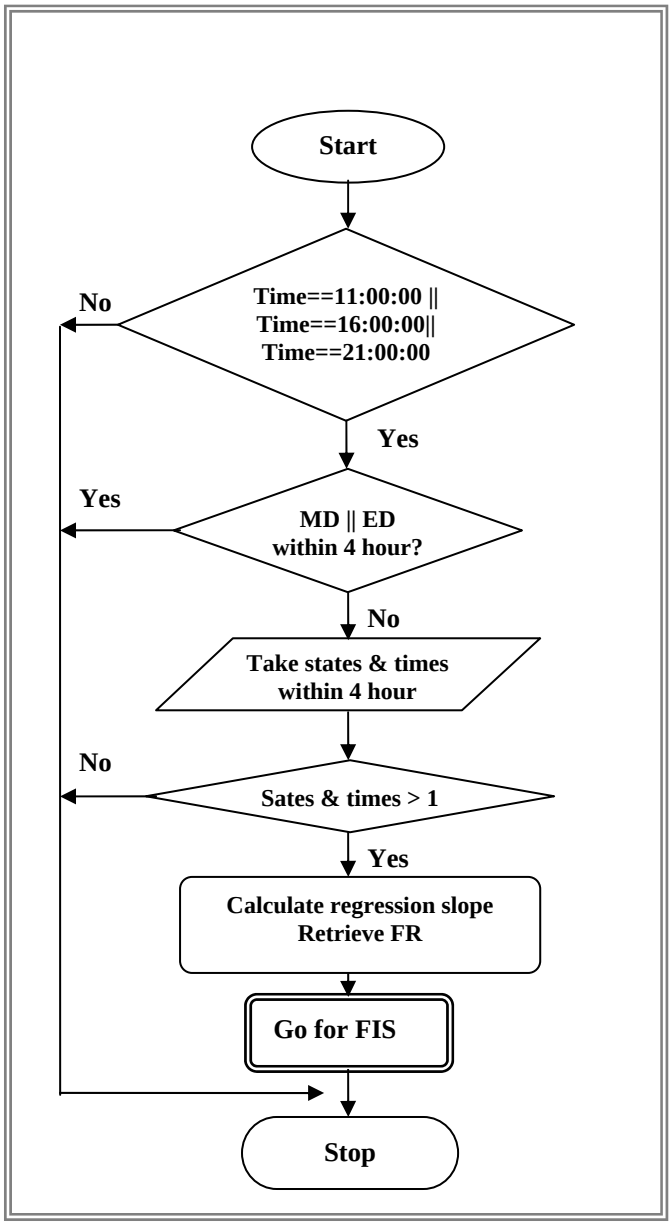


Figure 12: Flow chart for flow rate

Dose alerts

For three categories; extra dose, flow rate and daily dose alert was generated. System checked number of extra dose, number of flow rate changes and compared daily doses with previous

day. It calculated total doses in each day that patients were taking and check if total amount of daily doses was 20% less or 20% more than previous day then generated an alert. The flow chart of alert system is given in figure no 14:

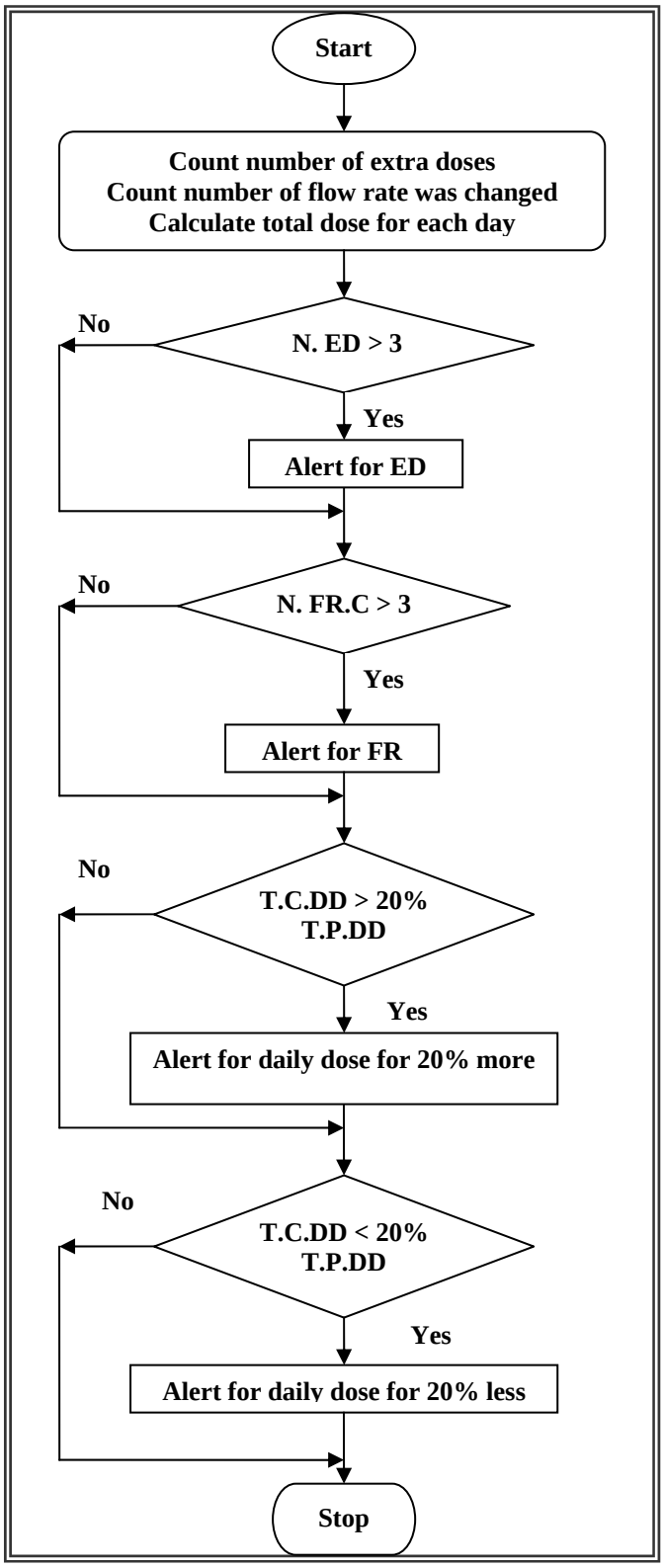


Figure 13: Flow chart for alert

3.3.2 Fuzzy inference system

Mamdani FIS has four steps: fuzzification of the input variables, rule evaluation, aggregation of the rule outputs and defuzzification. A single-input single-output Mamdani fuzzy model was extracted from the expert knowledge. Where state condition was taken as input variables and new dose was the output. Variable state was crisp but it was transferred into fuzzy variable and new dose was fuzzy variables with old dose but final output comes as crisp value by weighted average defuzzification.

- ***Fuzzy Rules***

The parameters of the IF–THEN rules (known as antecedents or premise in fuzzy modeling) define a fuzzy region of the input space, and the output parameters (known as consequent in fuzzy modeling) specify the corresponding output. Hence, the efficiency of the FIS depends on the number of fuzzy IF–THEN rules used for computation. Implemented rules can be written as:

Table 7: Rules of the mamdani fuzzy model

Rule no.	Antecedent	Consequent
	State	new Morning Dose (MD)
1	negative	MD + 20%MD (old dose)
2	positive	MD - 20%MD (old dose)
Rule no.	Antecedent	Consequent
	State	new Extra Dose (ED)
1	negative	ED + 20%ED (old dose)
2	positive	ED - 20%ED (old dose)
Rule no.	Antecedent	Consequent
	State (regression slope)	new Flow Rate (FR)
1	falling	FR + 20%FR (old dose)
2	rising	FR - 20%FR (old dose)

- ***Fuzzy Variables and MFs***

State condition and new dose were linguistic variables. Negative, positive, falling and rising were linguistic values determined by the fuzzy sets “RightLinearFuzzySet” and “LeftLinearFuzzySet” on universe of discourse state condition (or slop of regression). Increased and decreased were linguistic values determined by the fuzzy sets “SingletonFuzzySet” on universe of discourse new doses.

Plots of the membership functions of input state condition and regression slope with the universe of discourse [-5, 5] and [-5, 5] respectively is shown in figure no 15:

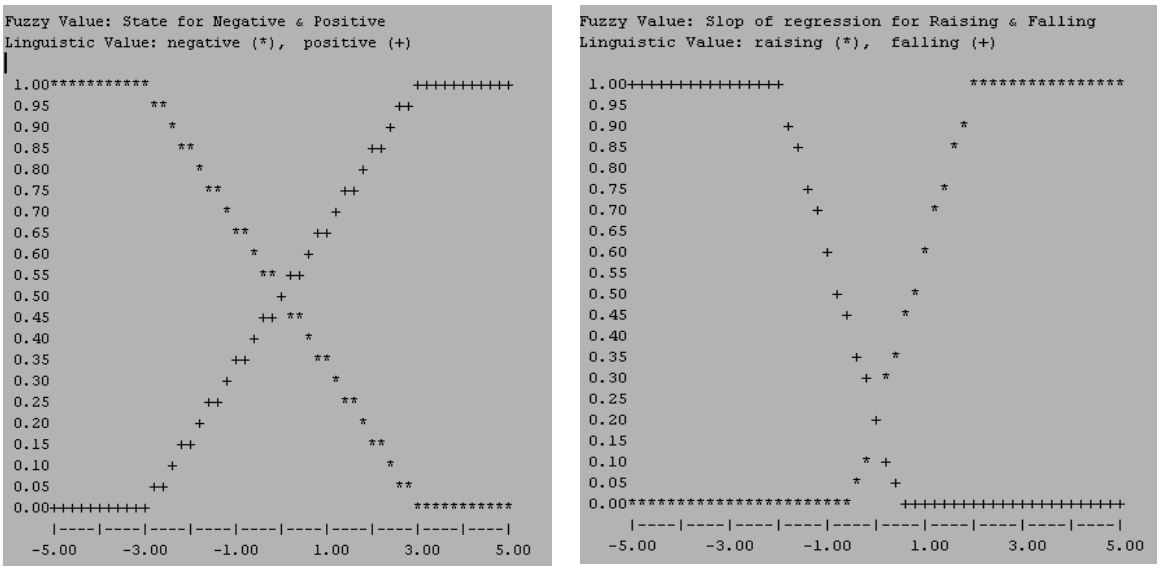


Figure 14: Antecedent state condition and regression slop MFs

In the figure no 15, fuzzy variable state was define with fuzzy set negative and positive and fuzzy variable regression slope was defined with fuzzy set falling and rising. Negative and positive were defined by right linear fuzzy set and left linear fuzzy set with parameters of membership functions [-3, 3] and falling and rising also were defined with same fuzzy set but different parameters [-2, 0.5] and [-0.5, 2].

Membership functions of new dose with the universe of discourse [0,15] respectively is shown in figure no 16:

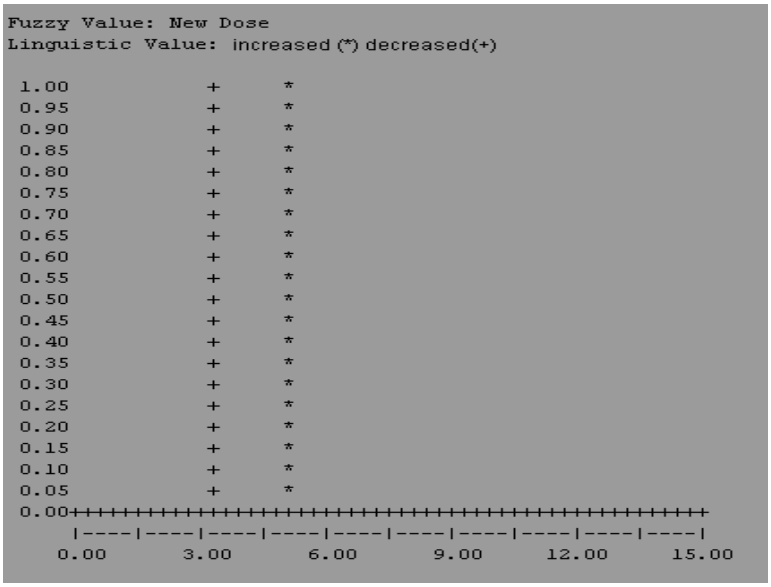
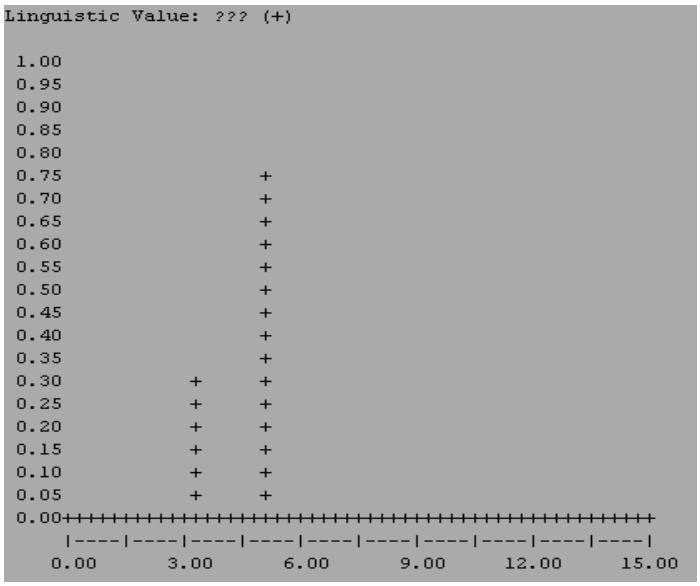


Figure 15: Consequent new dose MFs

20% decresed from the old dose value “4” was “3.2” and 20% increased from old dose value “4” was “4.8”. So, parameter for the member ship function was [3.8,4] and [4,4.8].

- ***Output***

To get new dose, input state condition was -1.5 and old dose was 4 which generated fuzzy set value after fuzzy union. Defuzzification extracts a crisp value from the fuzzy set. Output of the fuzzy union, fuzzy set value and weighted average defuzzified crisp value is shown figure no 17:




```
Fuzzy set for new dose valve change : FuzzyVariable        -> New dose     [ 0.0, 15.0 ] ml
Linguistic Expression -> ???
FuzzySet             -> { 0/3.2 0.31/3.2 0/3.2 0/4.8 0.77/4.8 0/4.8 }



weighted average defuzzify new dose valve : 4.3428571428571425
```

Figure 16: Output fuzzy union of MFs and crisp value

3.4 Testing

Decision support was tested with two different types of data sets, one was observation where DSS was build depend on those data and another one was clinical study that comes form DireQt study. System was checked with all business logic and fuzzy rules those were implemented, and it worked properly for both data sets. New advised information, alert and old doses summary were shown in the web pages with different search criteria. The web application was worked properly and it was made more users friendly to navigate different pages.

A mean difference and absolute mean difference were calculated for advised doses and taken doses. To get less difference membership function of fuzzy inference system was tuned. A table below describes tuning membership function for both observation and DireQt study data set.

Table 8: Differences in observation data

Parameter of MF	Mean difference	ABS mean difference
[-3.0, 1.0] [-1.0,3.0]	0.127	0.952
[-3.0, 2.0] [-2.0,3.0]	0.114	0.708
[-3.0,3.0] [-3.0,3.0]	0.080	0.673

Fuzzy sets, negative and positive states condition were tuned to each other with universe of discourse from [-3.0, 1.0] and [-1.0, 3.0] to [-3.0, 30] and [-3.0, 3.0]. Finally, it was found that less difference comes from [-3.0, 3.0] and [-3.0, 3.0] in both data sets.

4 Results

4.1 Web application

The web application consisted of pages with different search options: date wise, patient wise, dose wise and some chart pages. Most of the screen prints of page-layouts are included in the appendix, only main pages are described below:

4.1.1 Dose alert

This page showed most recent dose alerts per patient in different days. Initially 10 patients dose alert information were shown, sorted for most recent date and a navigation button were include to see more information. The layout is shown in figure no 18:

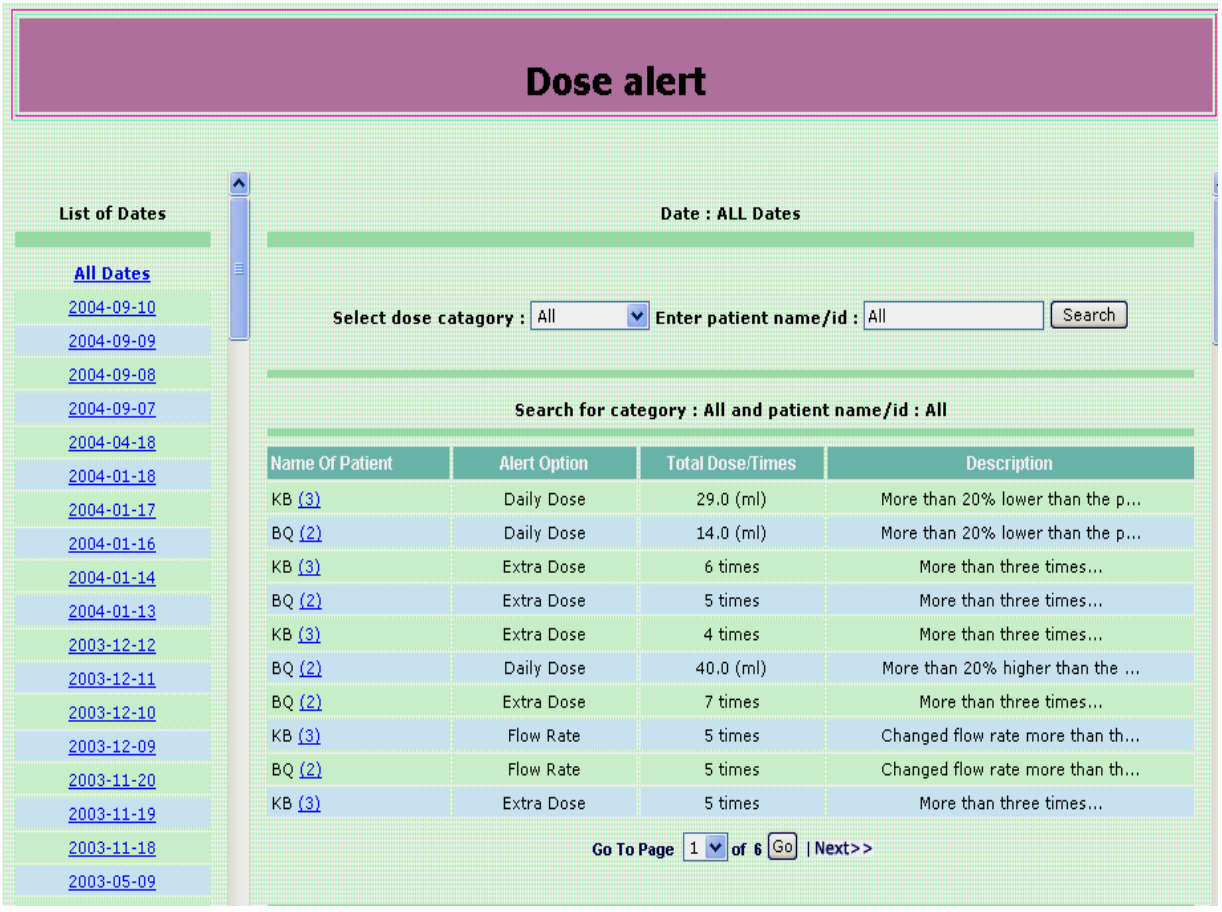


Figure 17: Dose alert page

On the left hand side all dates were listed and the right side listed alerts for all patients in all dose categories against selected date. Reason for generating the alert was also given. User can search with individual dose options for each patient and check detailed information about any patient.

4.1.2 Summary of doses

Summary of doses with maximum, minimum, mean and standard deviation for each patient in a given period was presented.

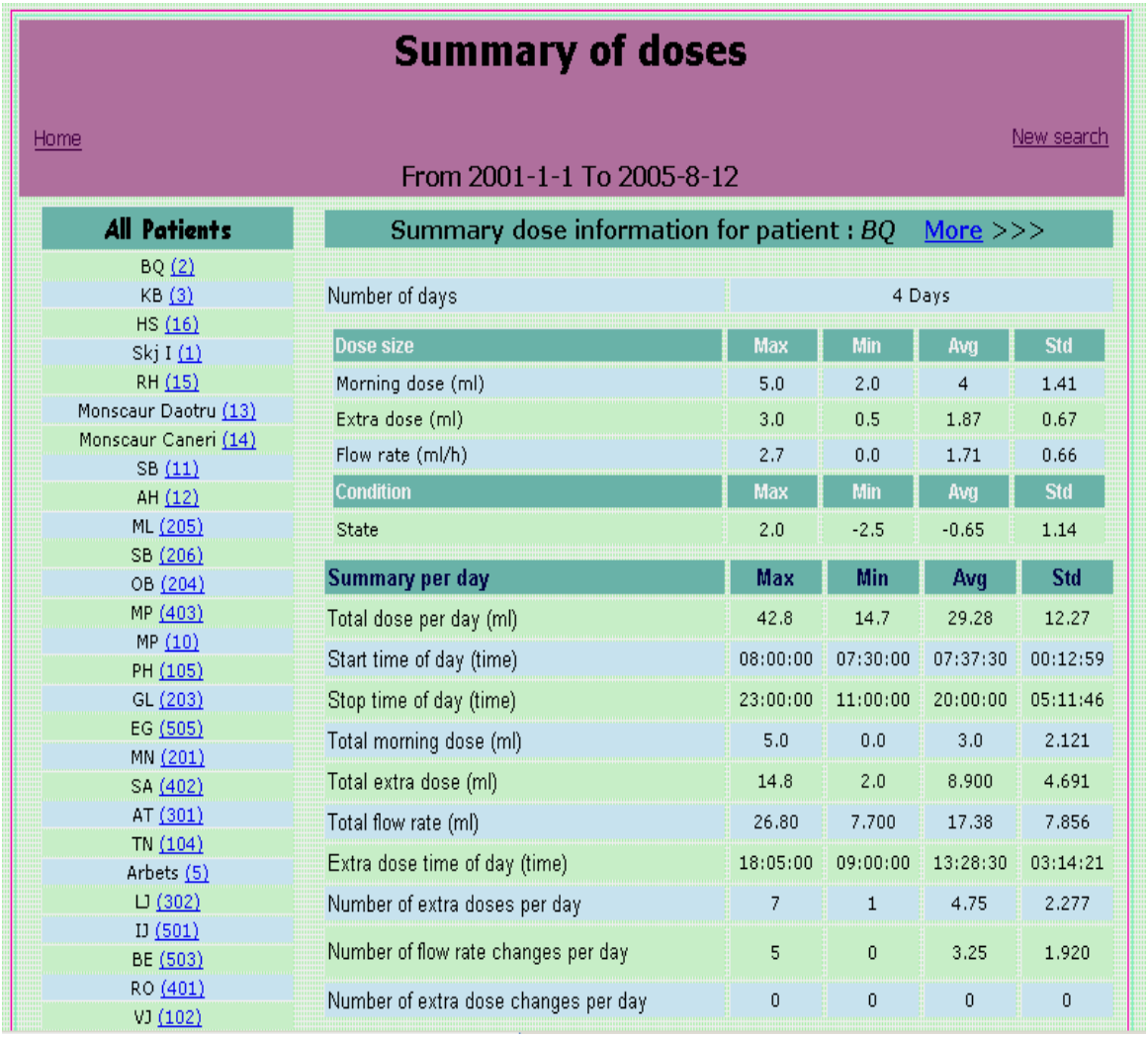


Figure 18: Summary of doses page

Chart diagram page with dose value and state condition against time for each patient in different days was included in this web application. Different colors were presenting different dose options and states as given on the TRS.

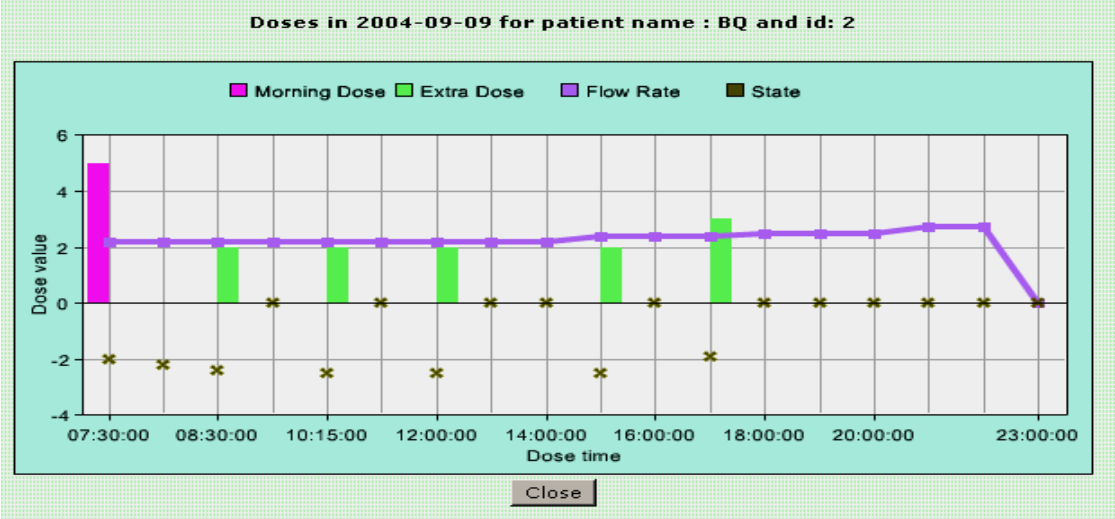


Figure 19: Chart for doses and states pages

4.1.3 Dose advice

This page listed new dose for dose adjustment that was an outcome of the decision support system. In this page, previous doses, states, new doses and advice reason with percentage of dose changes were presented.

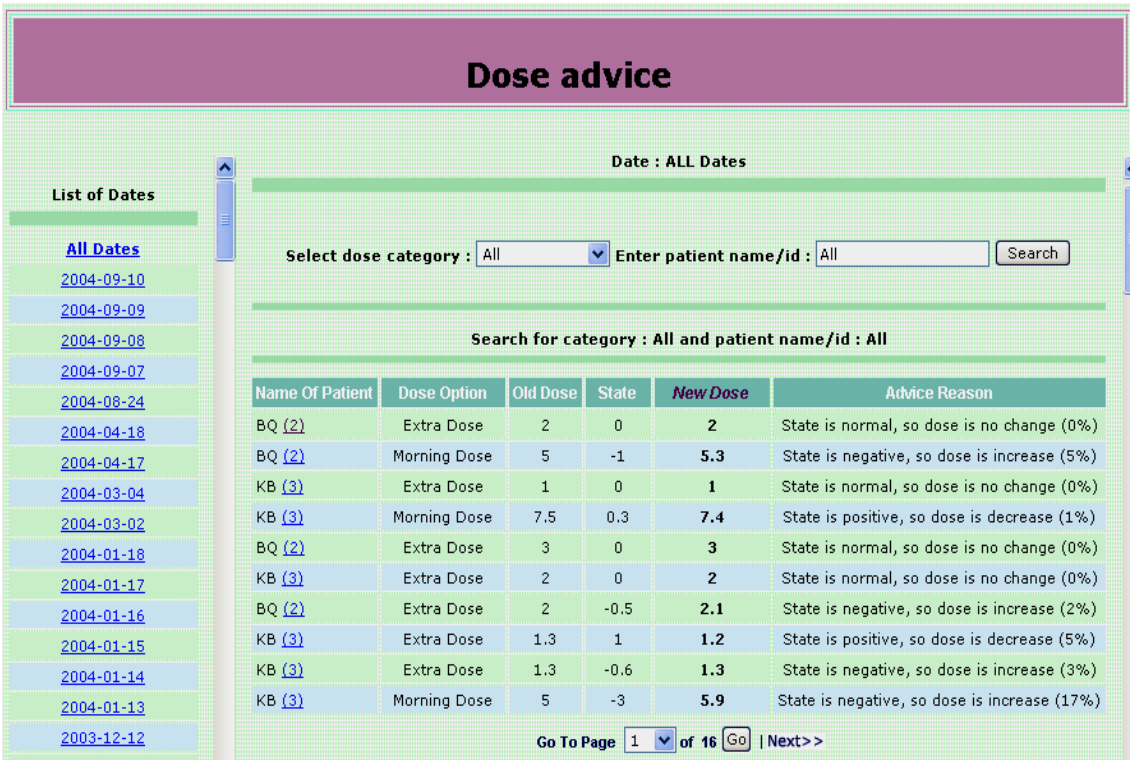


Figure 20: Doses advice pages

Search option were same as other pages but a comparison chart between previous dose and new dose value was included with different dose options for each patient in different days.

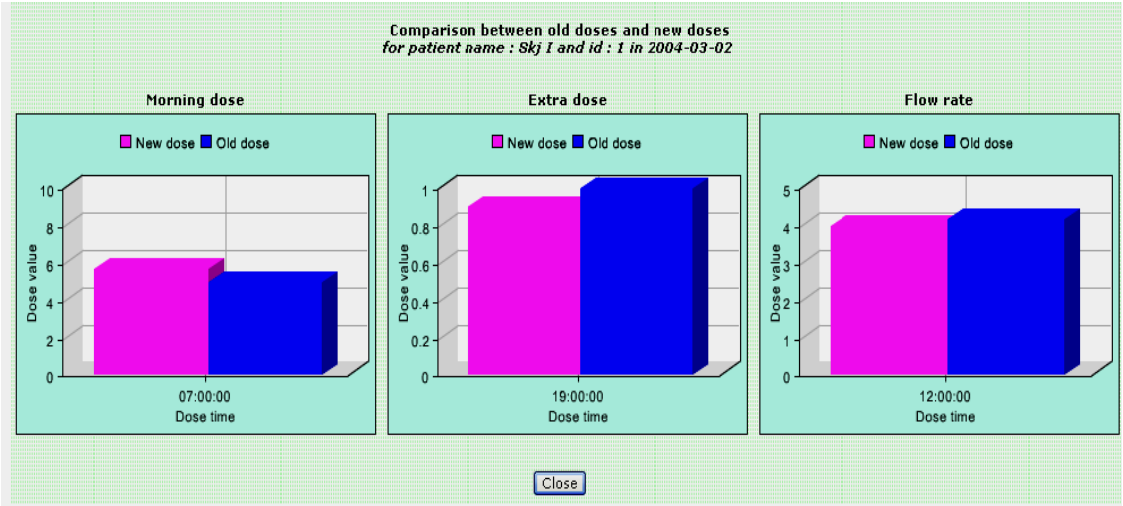


Figure 21: Chart for comarision among old doses and new doses

4.2 Decision support evaluation

New doses were generated and stored in particular time, after that time to the rest of the day; actual doses taken by the patients were checked and stored. Mean difference and mean absolute difference were calculated and plotted in bar diagram for each patient with different dose option in different days.

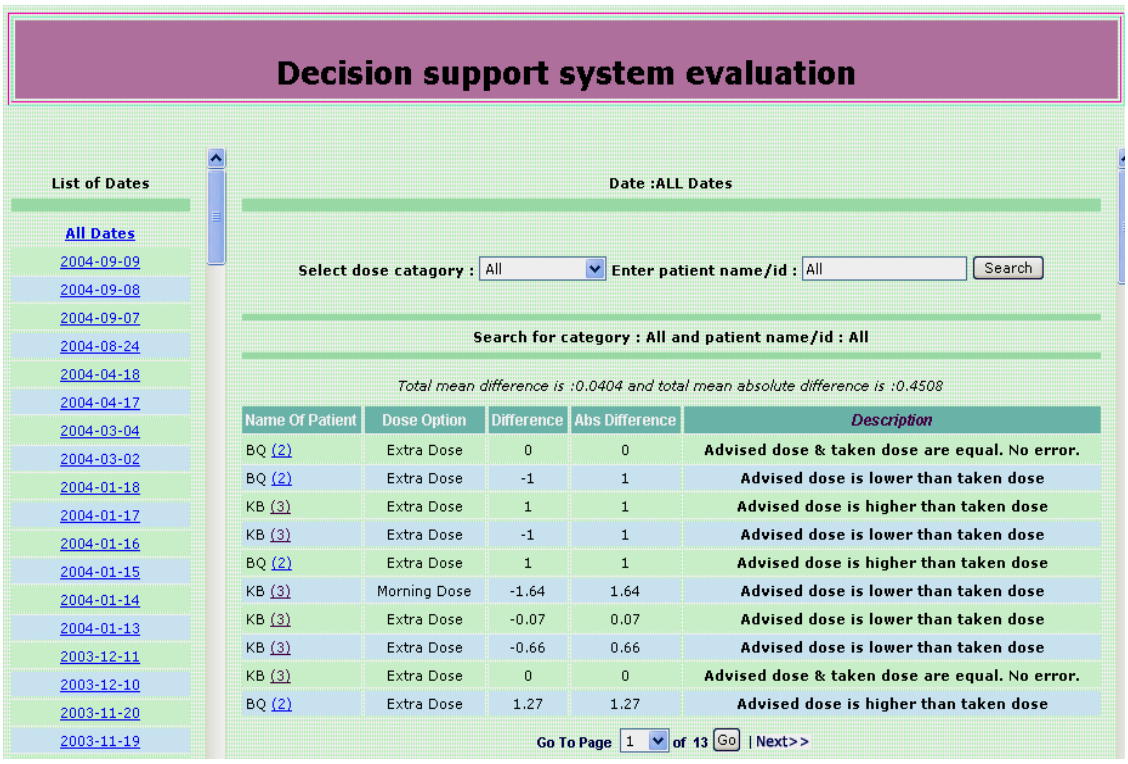


Figure 22: DSS evaluation with mean & ABS mean diffrence

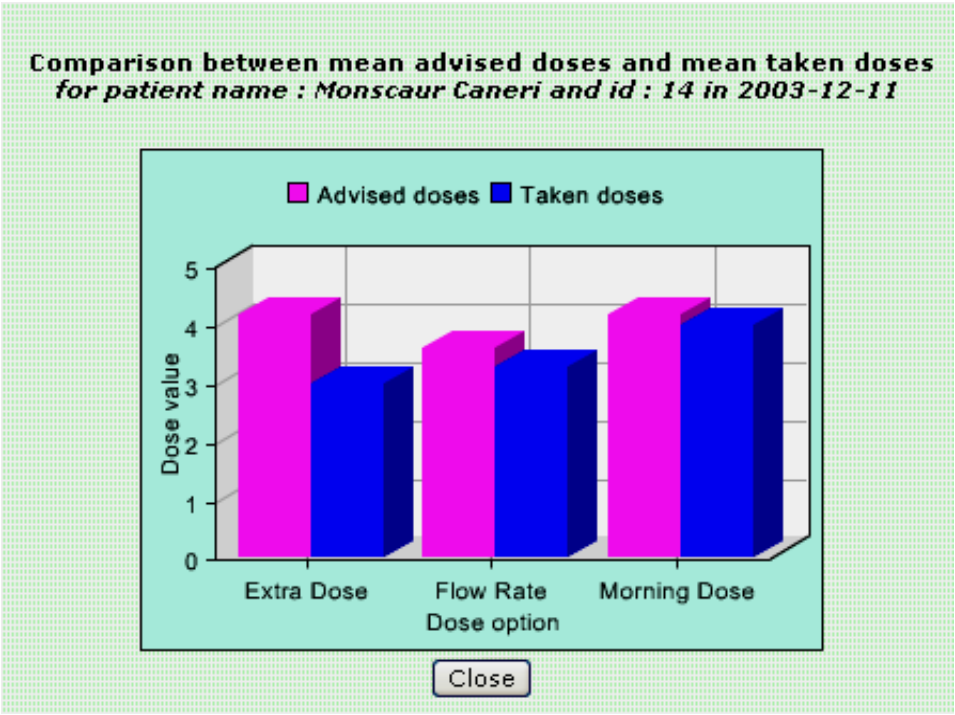


Figure 23: Chart for comparision among advised doses and taken doses

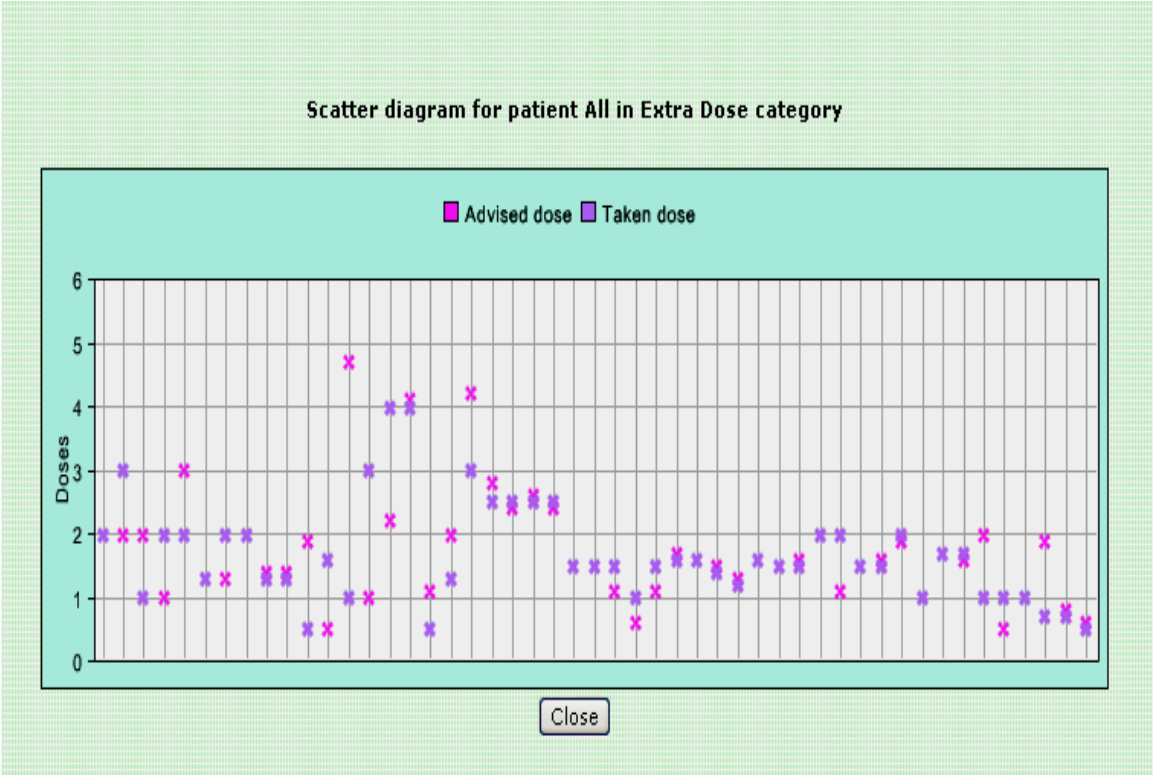


Figure 24: Scatter diagram for extra doses all patients

The decision support was evaluated with two different data sets individually and together in different dose categories. Scatter diagram of advised vs. taken doses was included.

4.2.1 Observation data set

Observation data were found as hard copy; based on those data and expert knowledge DSS was developed. Goodness of fit (R^2), mean difference and absolute mean difference between advised and taken doses were calculated for all dose categories: morning dose, extra dose, flow rate and for total data set. Evaluation and scatter diagram in different options are shown here:

Table 9: Evaluation for observation data

Dose option	Mean Diff.	ABS mean Diff.	R^2
Morning dose	0.27	1.58	0.25
Extra dose	-0.019	0.66	0.22
Flow rate	0.13	0.24	0.87
Total	0.08	0.67	0.65

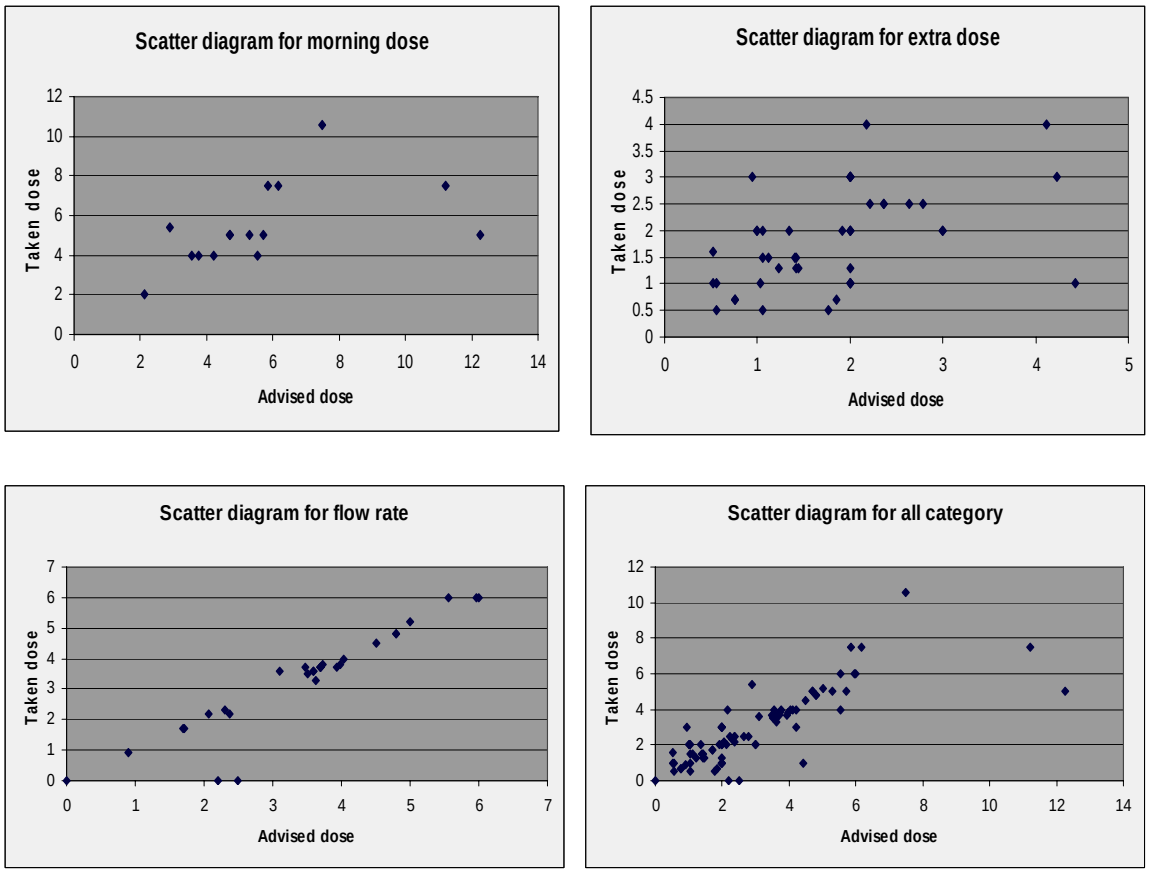


Figure 25: Scatter diagram total and different dose option

4.2.2 DireQt study data set

Decision support system was tested and evaluated with these data. Calculation of mean diffrence, absolute mean diffrence and square of the correlation coefficient (R^2) and scatter diagram of R^2 are shown here.

Table 10: Evaluation for test data (DireQt)

Dose option	Mean Diff.	ABS mean Diff.	R^2
Morning dose	Nil	Nil	Nil
Extra dose	-0.016	0.062	0.91
Flow rate	-0.014	0.17	0.97
Total	-0.015	0.14	0.98

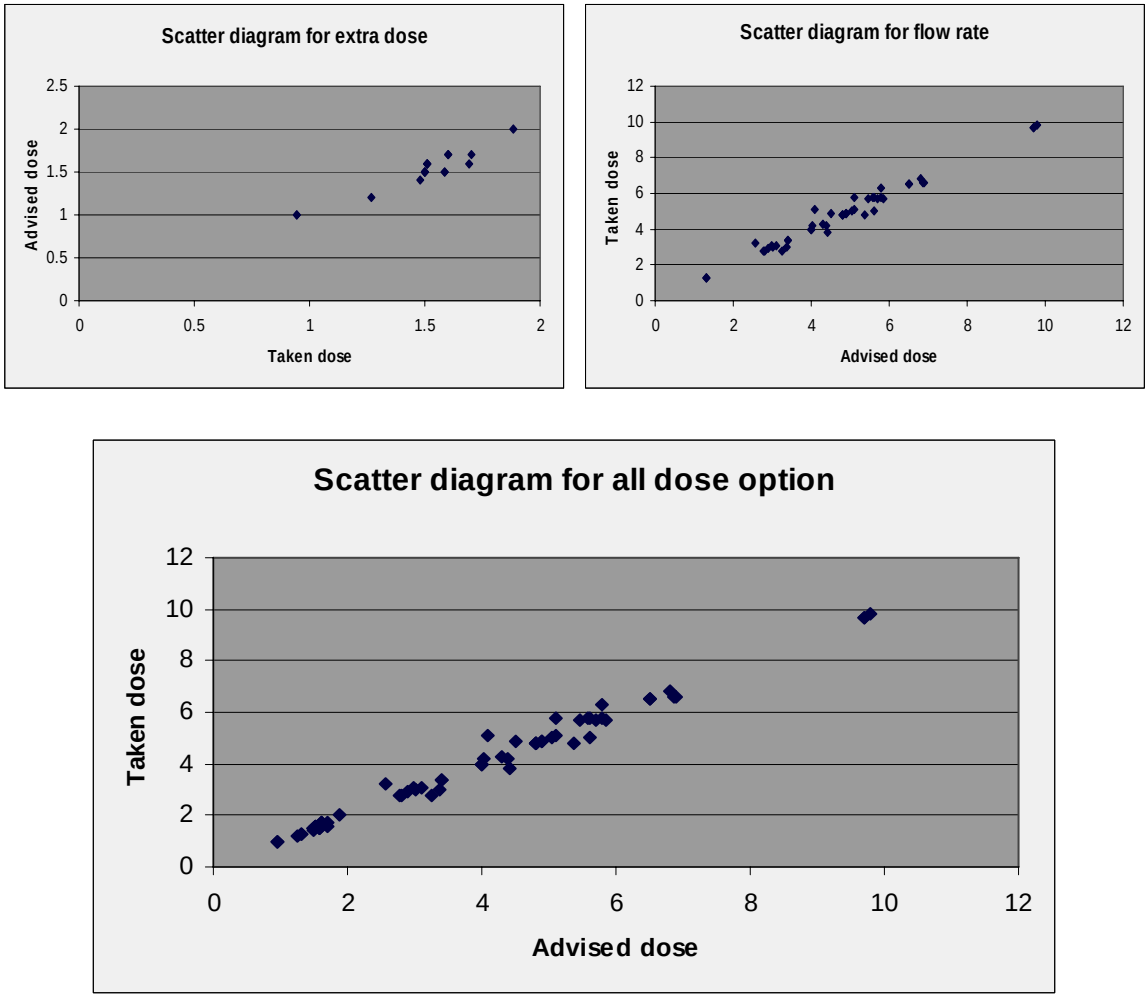


Figure 26: Scatter diagram total and different dose option

4.2.3 Combined data set

It was very interesting to see the performance of both data sets together. Scatter diagram of R^2 and table of different dose evaluation among all data set were given below:

Table 11: Evaluation for combination of both data sets for different doses

Dose option	Mean Diff.	ABS mean Diff.	R^2
Morning dose	0.27	1.59	0.25
Extra dose	-0.018	0.49	0.26
Flow rate	0.045	0.20	0.94
Total	0.041	0.45	0.81

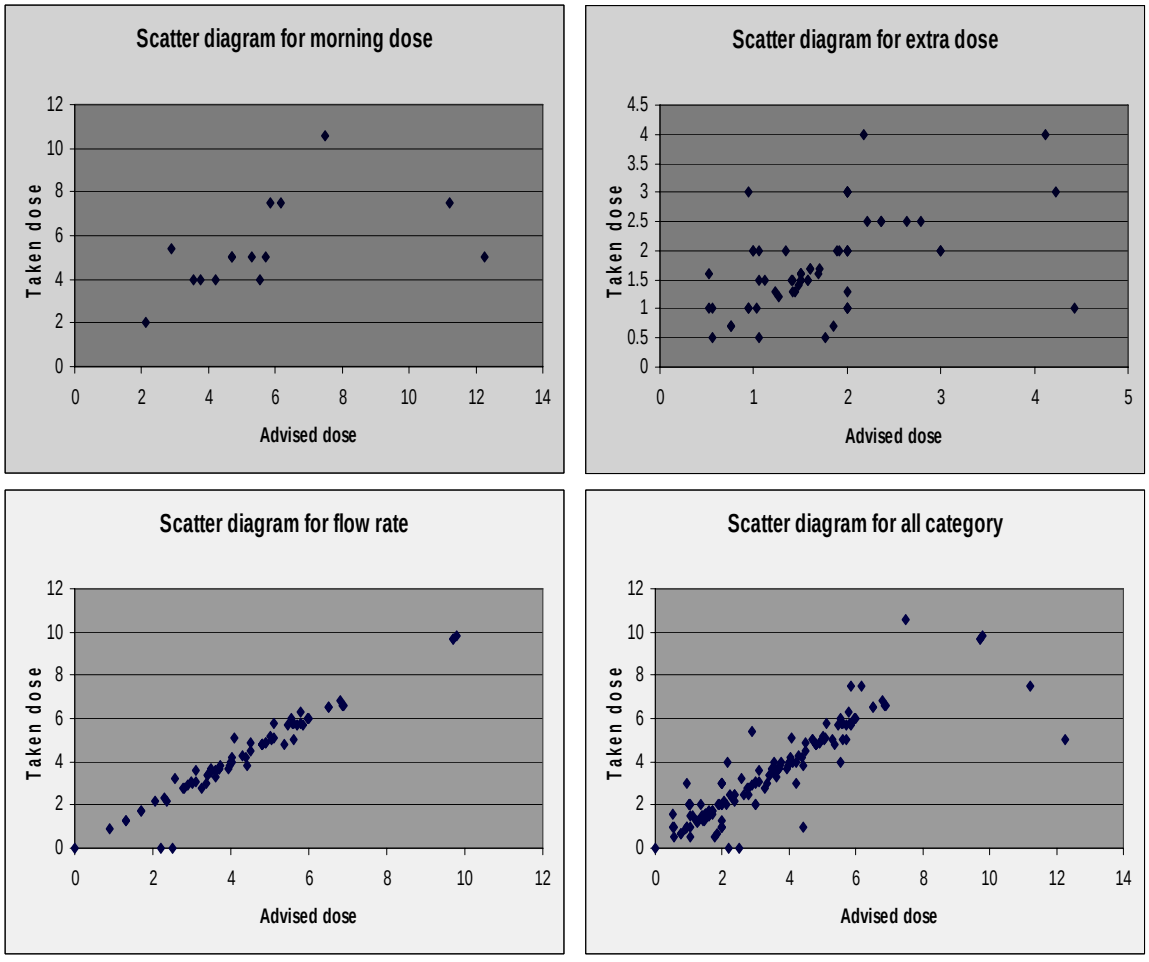


Figure 27: Scatter diagram of total and different dose options for combined data set

4.2.4 Observation data set without outliers

Performance of the DSS was also checked without the outliers in the observation data set and the results are shown in the following table.

Table 12: Evaluation for observation data without outliers

Observation data			
Data sets	**Mean Diff.**	**ABS mean Diff.**	**R^2**
Morning dose	-0.54	0.79	0.87
Extra dose	-0.009	0.53	0.45
Flow rate	-0.02	0.09	0.98
Average	-0.06	0.50	0.81

A brief discussion about the system with the above results is given in the discussion section where outliers points were investigated and effect of them in the result were discussed. Also limitation and some future works are described.

5 Discussion

The web enabled fuzzy rule-based decision support system was implemented for adjusting the doses in advanced PD would work as an assistant for the clinical staffs to make a decision.

User interface is an important thing for the DSS it should have a user friendly interface so that the user could interact with it easily. DSS provided information for advised doses, dose alert and summary of dose. All these information would help the clinical staffs for taking the decision. In result sections (Section 4.1 Web application) some of the web pages were given where different search options gave the facility to the user to search by different options; by date, by patients, by doses etc. For different purposes result were interpreted using graphical presentation; using bar chats, scatter diagram etc. that would help to realize the situation easily. For dose advice it gave the advised dose amount for each patient for all doses (extra dose, flow rate and morning dose) and at the same time it described the reason behind the given dose amount, which would be so helpful to get the knowledge. Also for generating dose alert the reason i.e. the situation of the patient was described which might be interesting to know in many cases. From dose summary and dose alert clinical staffs could monitor patient's dose information.

Using this DSS user could also check the *performance of the system* i.e. how it advised in order to get an optimal dose amount which was very important to evaluate the system. In result section (Section 4.2 DSS evaluation) comparison between the dose advised by the DSS and the dose already taken by the patients was shown using bar charts (figure no. 24) and scatter diagram (figure no. 25) for a patient in a specific date. Observation data set (new patients) used to design DSS and goodness-of-fit, mean difference and absolute mean different were calculated (table no. 9) for this data set. Goodness-of-fit for the morning dose and extra dose were much less than flow rate. It showed that system implemented 87% of the expert's knowledge in case of flow rate but for morning dose and extra doses it was just 0.25% and 0.22% respectively. Corresponding mean difference and absolute mean difference also showed that in case of flow rate these differences were lower comparatively with other doses. Finally, it found that average goodness-of-fit from observation data set was 65% in case of all dose categories. Corresponding scatter diagram for total and different dose options are shown in figure no. 26.

In order to check the *performance of DSS for another data* set instead of observation data DireQt study data were used where information about ongoing patients for advanced Parkinson's disease were stored. Information for the morning dose was missed here (Table no. 10) because of the study was a crossover study where test information was taken in two different test days, as it must be given in every morning so it was not possible to compared without the continuous dose information. Goodness-of-fit for the flow rate and extra dose was 97% and 91% which showed that it could implement the expert's knowledge much better in case of these doses compared with the observation data (new patients). Corresponding scatter diagram in figure no. 27 also support this.

Moreover goodness-of-fit was calculated for the overall data sets; observation and DireQt study data (new and ongoing patients). Result showed (Table no. 11) that average goodness-of-fit was 81%.

It was found that the *difference between the taken doses and advised doses for the new patient's were comparatively lower than ongoing patients*. One of the main reasons behind this was that the ongoing patient's were already set up i.e. doses were already adjusted for these patient's which was not true for a new patient. For new patients some experimental doses were given at the beginning so that patient can reach a steady-state concentration and after that the infusion rate was adjusted to maintain this concentration level. Because of both cases; new and ongoing patients flow rate level were adjusted when patients would reach a steady-state concentration level, the difference between the taken doses and the advised doses for flow rate was comparatively lower than other doses and this difference was much clear for new patients. It can also be noticed from the scatter diagram of figure no. 26 and figure no. 27.

For new patients from the scatter diagram (figure no. 26), it was found that some of the observations were distinct from the main body of the data and were incompatible with the rest of the data points. The outlying observations were patient ids 3, 7 and 15. The reason of their appearances was investigated and it was found that the state conditions for them fluctuated very much compared with the other patients. For these outliers it was noticed that due to unusual health conditions (patients were in negative state) of these patients at the beginning of their treatment, they were treated with many extra doses. It was also interesting to check the *effect of these outliers* in the result. For an experiment, evaluation was done again for different doses without the outliers and found (Table no. 12) the goodness-of- fit which were 87%, 45% and 98% for morning doses, extra doses and flow rate respectively. On average it was 81% but with outliers it was 65%. Goodness-of-fit for the overall data; for new and ongoing patients on average was 91% which was better than (81%) with outliers.

So the system was verified according to the requirements specification and the evaluation result of how accurately it could achieve the expert's knowledge for this domain is discussed. In order to *design the system* it was also important to think about the architecture of the system so that necessary modification could be done in future. Here, DSS was designed in three tire architecture that provided facilities for the developer and user for future modification. The advantage of this kind of architecture is that any kind of modification can be done easily because all the layers were working individually. For example, fuzzy member ship functions were tuned that was done in middle layer without any change in other layers. Some modifications were also done in web application (front end) for make it user friendly and present sufficient information on pages where other layers remained unaffected. Another advantage of this architecture is that back-end can be replaced with any databases like Microsoft Access, SQL Server, Oracle etc. and like this front-end can also be changeable with other kind of web-applications such as ASP, JSP, PHP etc.

For *implementing the expert knowledge* mamdani FIS was used. Mamdani fuzzy inference model is the most commonly used fuzzy inference technique. It has widespread acceptance and it's well-suited to human input. The rule structure of the system makes it easy to incorporate human expertise about the target system.

The DSS would start to adjust all the doses from the beginning; it was not waiting for dose adjustment until patients come in normal/positive state condition. The DSS could be helpful to get advice for all the doses at the beginning of their treatment for new patient and ongoing patients. This might give a quick and better response of the treatment. Also in Parkinson's disease dose adjustments were done individually for each patient and normally it takes time for calculating the measurement for dose adjustment, as this developed DSS is a computerized automated systems it an calculate quickly and could help the clinical staffs providing the necessary advice for individual patients.

5.1 Limitations

In this system there was no option to add/modify the rules that used here for fuzzy inference system. Actually rules for the FIS were defined by the experts. General users (Clinical staffs) for this DSS are not allowed to add/modify the rules. It might depend on the interest of the researcher in this area to do this add/modify in fuzzy rules so it is out of the purpose of this work. But it could be done by recompiling the business layer after adding/modifying the rules.

Currently, there is no control over the incoming data. Because it was undefined how data will come into the database. In that case some data validation and some alert system could be a better approach for improving the performance of the system. In that case modification can be needed only in the front-layer.

5.2 Future work

In future for the real life data could possible to use ANFIS (Adaptive Neuro-fuzzy) for tuning the parameters of the membership function to see whether could get any improvement in the result. Also can generate alert for the state by watching the condition of the state.

System has been developed according to specifications. But validation of the system i.e. right system has been developed for its purpose is a necessary step which needs to be applied for this DSS. For this DSS it is a running process and already sent to some clinical staff's for user's evaluations. In future we would like to implement this web-based decision support system to real life application in a clinical study.

6 Conclusion

Computer-based decision support systems will play an increasingly important role in medical domain. They may improve the quality of the process in accuracy and efficiency. Potential users of this DSS could get the support for taking decision through alerts, monitoring etc. All the below points are decision making assistance that included in the system.

Dose advice: this system could assist the doctor/user for individually adjusting the dose amount of Dudopa and also explained the reason behind this which is very important for taking the decision.

Generating alerts: system could warn of changes in a patient's condition. In abnormal circumstances, it might check number of extra doses, number of flow rate changes and compare current dose with the previous doses and generate an alert.

Monitoring: clinical staff could monitor dose information for each patient by using the summary and alert information generated by the system. It could be searched and retrieved information for different time periods.

Initial dose calculation: could calculate initial settings of Morning dose, Flow rate and Extra dose based on current oral levodopa/carbidopa doses.

System Evaluation: system could do the evaluation between the dose advised by the system and the dose taken by the patient which might be interesting to see in many cases.

This DSS would help the clinical staffs by providing the necessary advice in order to optimize the doses in advanced PD with lower side effects and also gave them alert if any abnormal situation rose. Fuzzy logic technique helped to provide optimal amount of dose advice and quickly adjusted the doses where all the doses were tuned at the same time. Web-application with easy navigation of the pages makes it user-friendly. Within the DSS tried to incorporate the human knowledge using the artificial intelligence approach; fuzzy rule-based reasoning but it is important that it would just work as an assistant but not replacement of the clinical staffs.

Specification of the system's function was based on the users need in the problem at hand. One feature integral to the development is the need for user evaluation before goes to real-life implementation. This has motivated to perform future work for user evaluation; means assessment of the object of evaluation, i.e. the decision support system does the right thing right. This evaluation might give us information on how the DSS influence the patients and professionals of that organization, as well as information concerning the economic and technical aspects of the system. In order to be a successful decision support system for this application domain satisfaction of the potential users would be the main concern.

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Appendix A

A.1 Database script:

```
Drop database DSS;
Create database DSS;
Use DSS;

CREATE TABLE tblPatient(
patientID INT(5),
PRIMARYKEY (patientID),
patiantName VARCHAR(250),
TScale INT(1)
) Type =INNODB;

CREATE TABLE tblDose(
doseID INT(5),
PRIMARYKEY (doseID),
Date DATE,
DoseTime TIME,
MorningDose FLOAT(13,12),
ExtraDose FLOAT(13,12),
Flowrate FLOAT(13,12),
state FLOAT(13,12),
patientID INT(5),
FOREIGNKEY (patientid)
REFERENCES tblPatient (patientid)
) Type =INNODB;

CREATE TABLE tblNewDose(
newDoseID INT(5),
PRIMARYKEY (newDoseID),
DoseDate DATE,
DoseOption VARCHAR(250),
DoseTime TIME,
OldDose FLOAT(13,12),
State FLOAT(13,12),
StateTime TIME,
NewDose FLOAT(13,12),
AdviceReason VARCHAR(250),
FOREIGNKEY (doseID)
REFERENCES tblDose (doseID)
) Type =INNODB;

CREATE TABLE tblEvaluation(
evluationID INT(5), PRIMARYKEY
(evluationID),
DateValue DATE,
DoseOption VARCHAR(250),
AdviceDose FLOAT(13,12),
TakingDose FLOAT(13,12),
Error FLOAT(13,12),
ABSError FLOAT(13,12),
Description VARCHAR(250),
FOREIGNKEY (patientid)
REFERENCES tblDose (patientid),
FOREIGNKEY (doseID)
REFERENCES tblPatient (doseID)
) Type =INNODB;

CREATE TABLE tblDoseSummary(
summaryID INT(5),
PRIMARYKEY (summaryID),
NameOfPatient VARCHAR(250),
DateValue DATE,
SummaryOption VARCHAR(250),
SummaryDose FLOAT(13,12),
SummaryTime TIME,
FOREIGNKEY (patientid)
REFERENCES tblDose (patientid)
) Type =INNODB;

CREATE TABLE tblAlert(
alertID INT(5),
PRIMARYKEY (alertID),
NameOfPatient VARCHAR(250),
DateValue DATE,
AlertOption VARCHAR(250),
TotalDoseInTime VARCHAR(250),
Description VARCHAR(250)
FOREIGNKEY (summaryID)
REFERENCES tblDoseSummary
(summaryID)
) Type =INNODB;

LOAD DATA LOCAL INFILE '/DSS/tblPatient.txt' INTO TABLE tblPatient;

LOAD DATA LOCAL INFILE '/DSS/tblDoseM.txt' INTO TABLE tblDose;

LOAD DATA LOCAL INFILE '/DSS/tblDose.txt' INTO TABLE tblDose;
```

Appendix B

B.1 User interface:

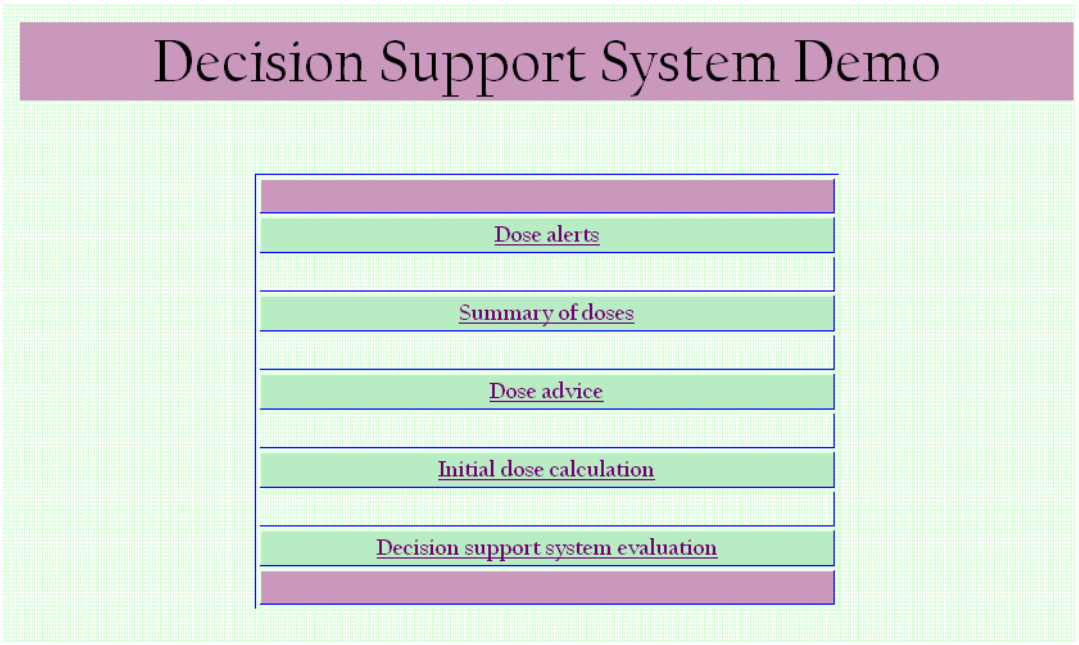


Figure B.1: Main Page of Decision Support System

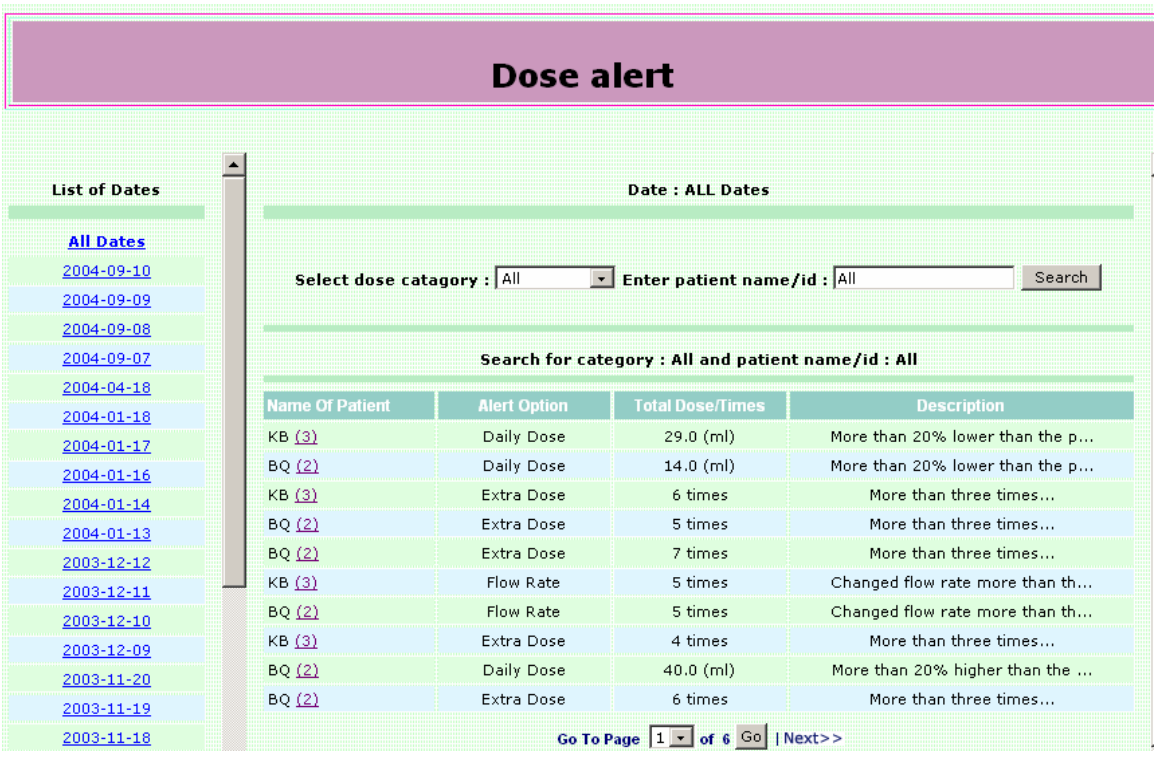


Figure B.1.1: Dose alert page

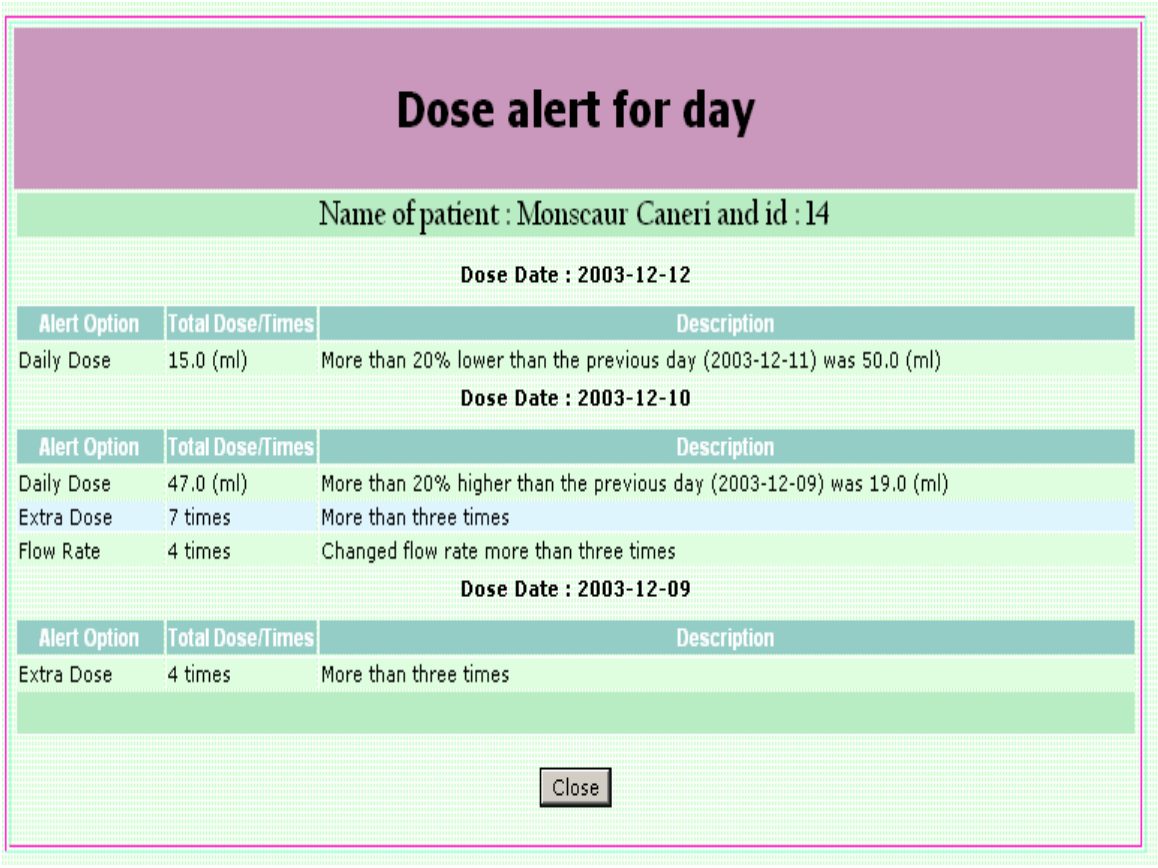


Figure B.1.2: Dose alert for day for a specific patient

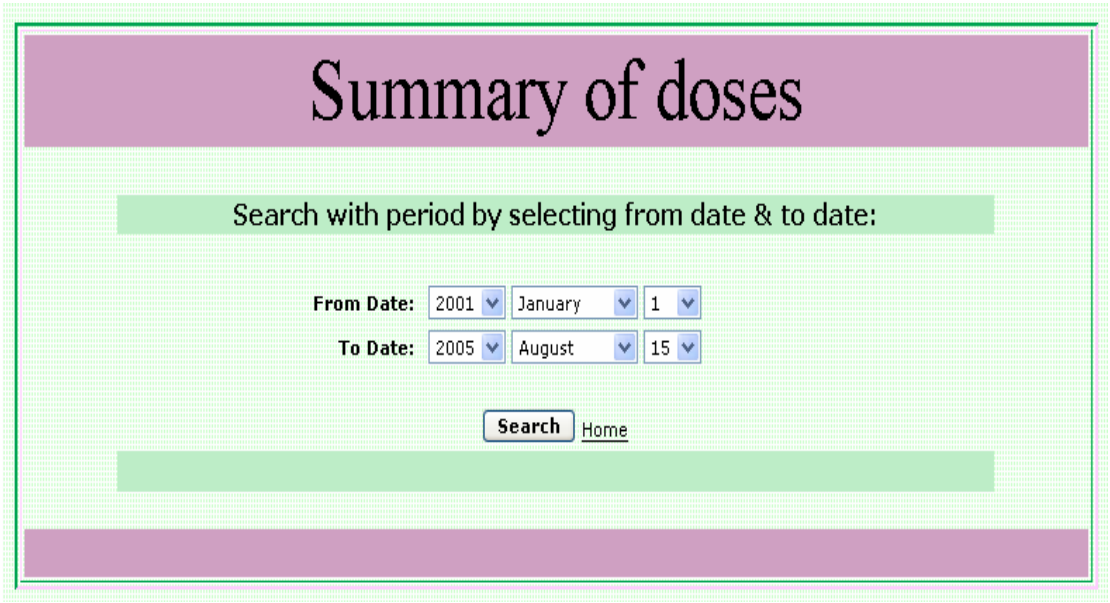


Figure B.1.3: Summary of doses page

Summary of doses

Home

New search

From 2001-1-1 To 2005-8-15

All Patients

BQ (2)
KB (3)
HS (16)
Skj I (1)
RH (15)
Monscaur Daotru (13)
Monscaur Caneri (14)
SB (11)
AH (12)
ML (205)
SB (206)
OBJ (204)
MP (403)
MP (10)
PH (105)
GL (203)
EG (505)
MN (201)
SA (402)
AT (301)
TN (104)
Arbets (5)
LJ (302)
IJ (501)
BE (503)
RO (401)
VJ (102)

Summary dose information for patient : *BQ* More >>>

Number of days	4 Days

Dose size	Max	Min	Avg	Std
Morning dose (ml)	5.0	2.0	4	1.41
Extra dose (ml)	3.0	0.5	1.87	0.67
Flow rate (ml/h)	2.7	0.0	1.71	0.66

Condition	Max	Min	Avg	Std
State	2.0	-2.5	-0.65	1.14

Summary per day	Max	Min	Avg	Std
Total dose per day (ml)	42.8	14.7	29.28	12.27
Start time of day (time)	08:00:00	07:30:00	07:37:30	00:12:59
Stop time of day (time)	23:00:00	11:00:00	20:00:00	05:11:46
Total morning dose (ml)	5.0	0.0	3.0	2.121
Total extra dose (ml)	14.8	2.0	8.900	4.691
Total flow rate (ml)	26.80	7.700	17.38	7.856
Extra dose time of day (time)	18:05:00	09:00:00	13:28:30	03:14:21
Number of extra doses per day	7	1	4.75	2.277
Number of flow rate changes per day	5	0	3.25	1.920
Number of extra dose changes per day	0	0	0	0

Figure B.1.4: Summary of doses for all patients for a time period

Summary of doses per day

Name of patient : BQ and id : 2

Date : 2004-09-10

Raw data chart

Summary Option	Summary Value
Start time of day	07:30:00
End time of day	11:00:00
Total daily dose	14.7
Total flow rate	7.7000003
Total morning dose	5.0
Total extra dose	2.0
Number of extra doses	1.0
Extra dose time of day (average)	09:00:00
Number of extra dose changes	0.0
Number of flow rate changes	0.0

Date : 2004-09-09

Raw data chart

Summary Option	Summary Value
Start time of day	07:30:00
End time of day	23:00:00
Total daily dose	42.8
Total flow rate	26.800001
Total morning dose	5.0
Total extra dose	11.0
Number of extra doses	5.0
Extra dose time of day (average)	12:49:00
Number of extra dose changes	1.0
Number of flow rate changes	4.0

Figure B.1.5: Summary of doses for a patient for each day

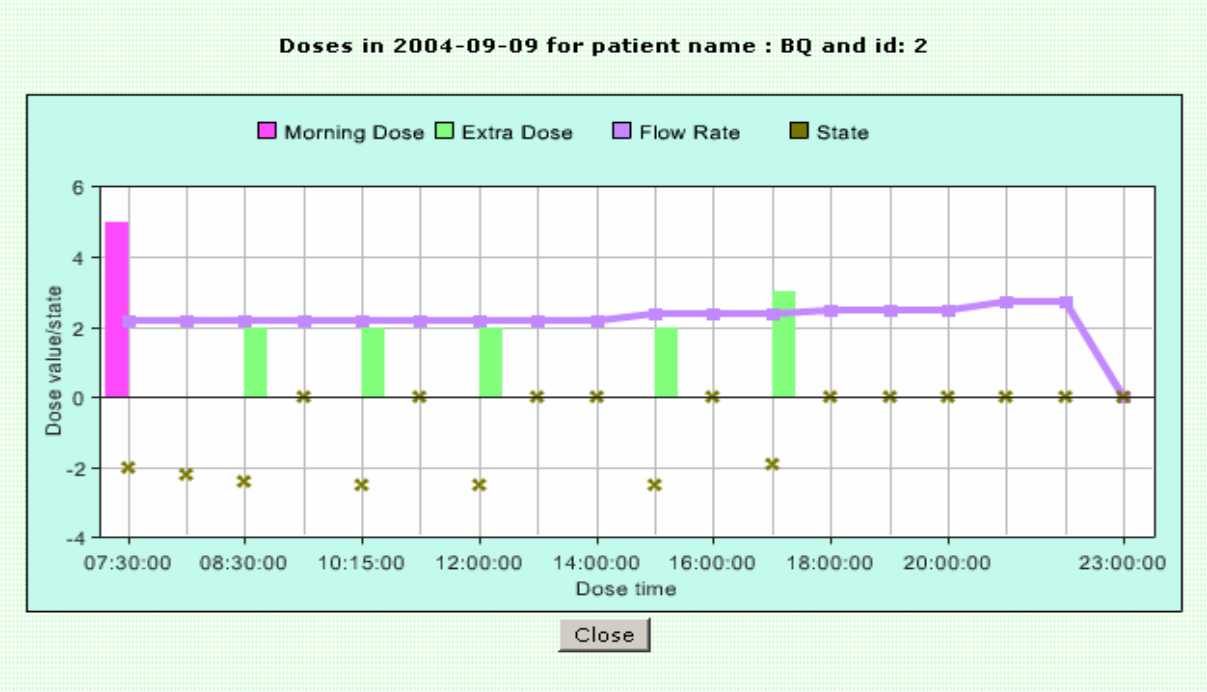
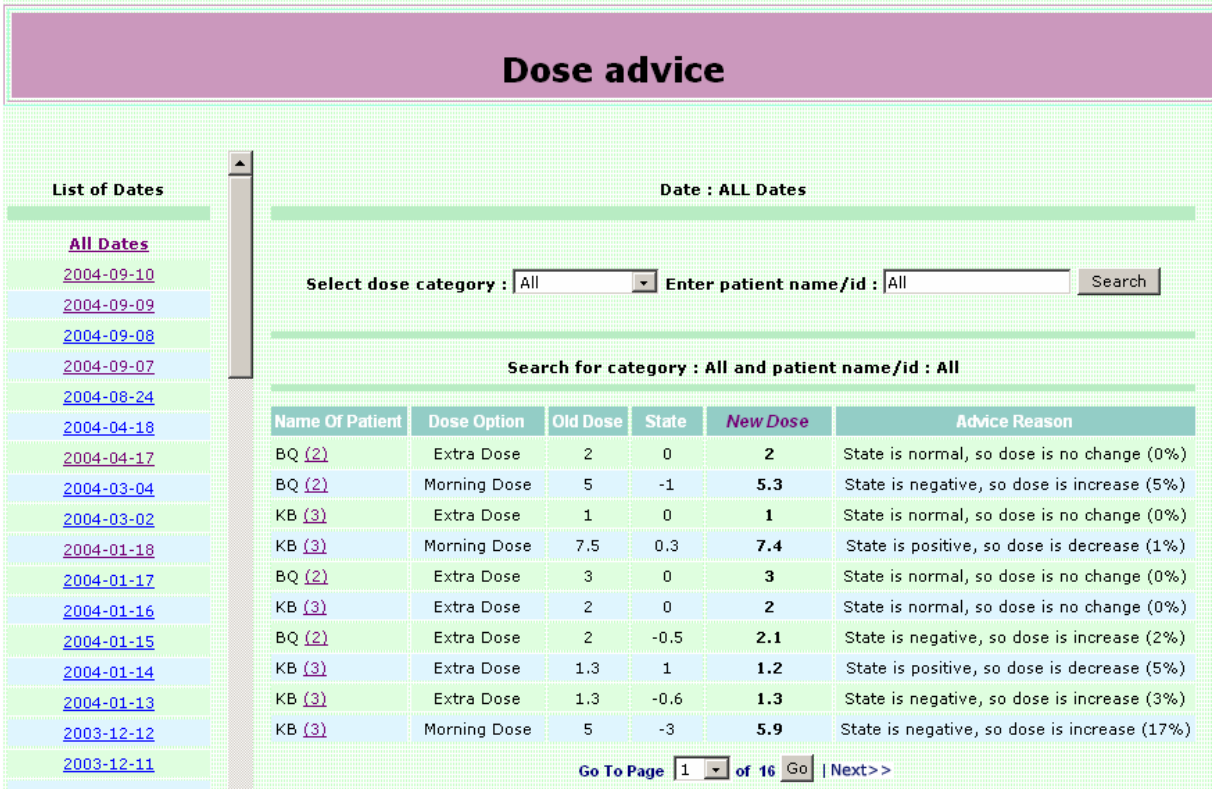


Figure B.1.6: Graphical presentation of summary of doses for a patient



FigureB.1.7: Dose advice page

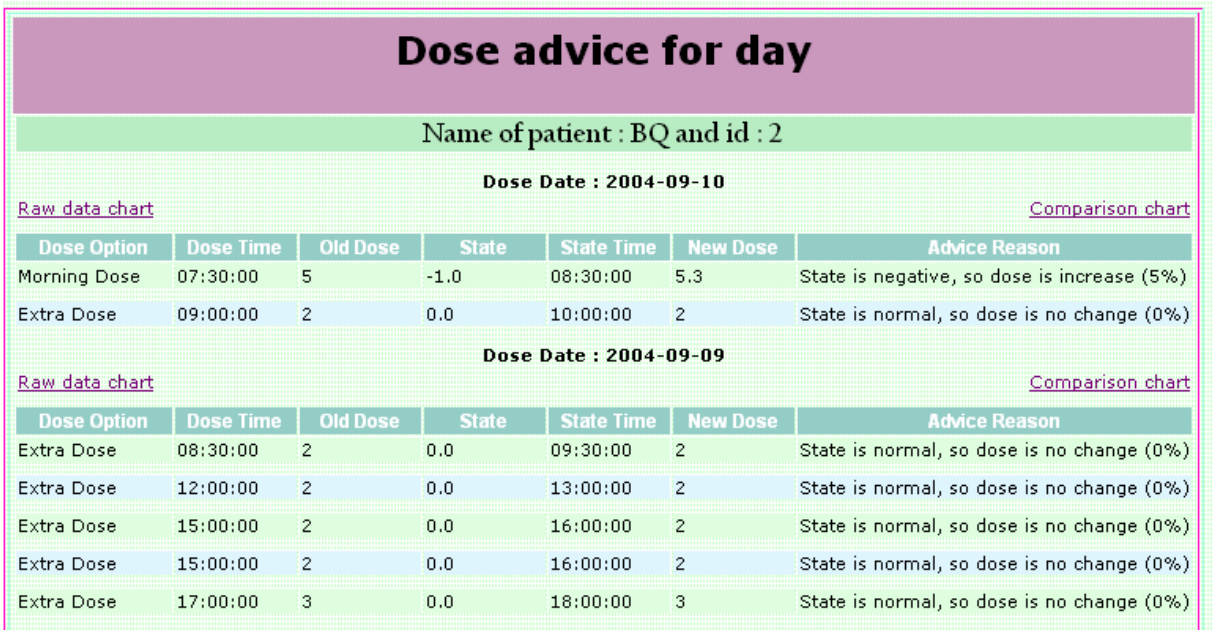


Figure B.1.8: Advice dose for a patient for each day

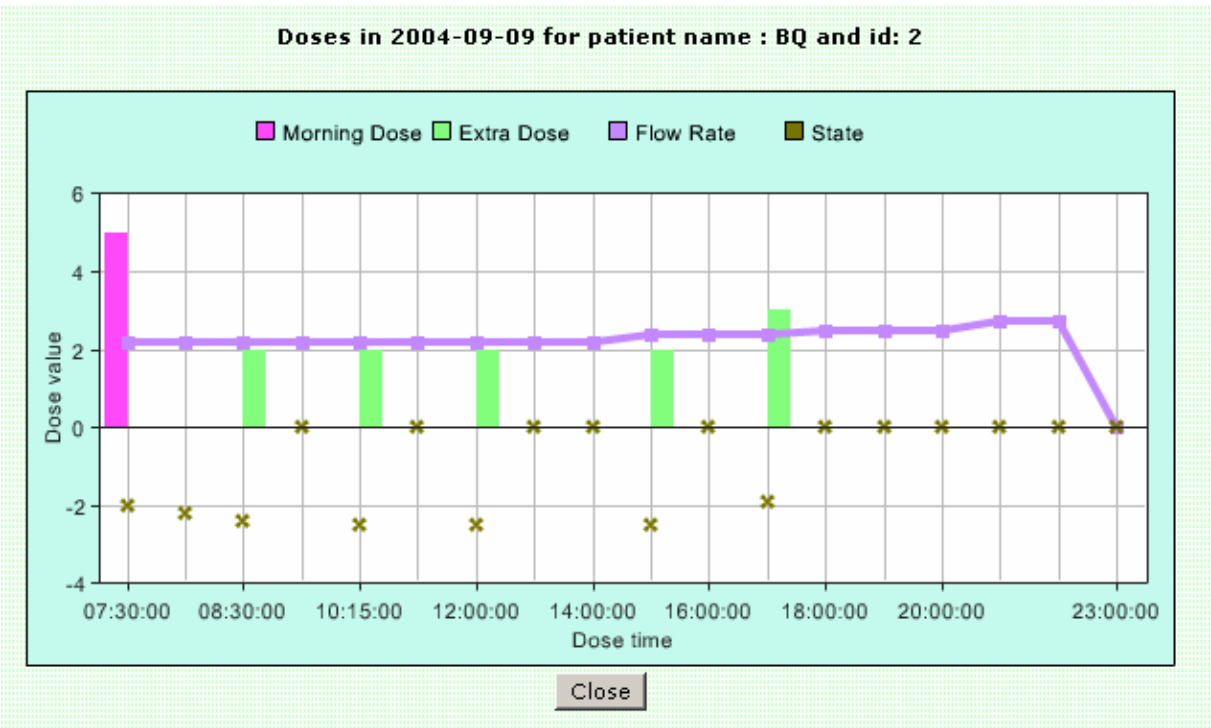
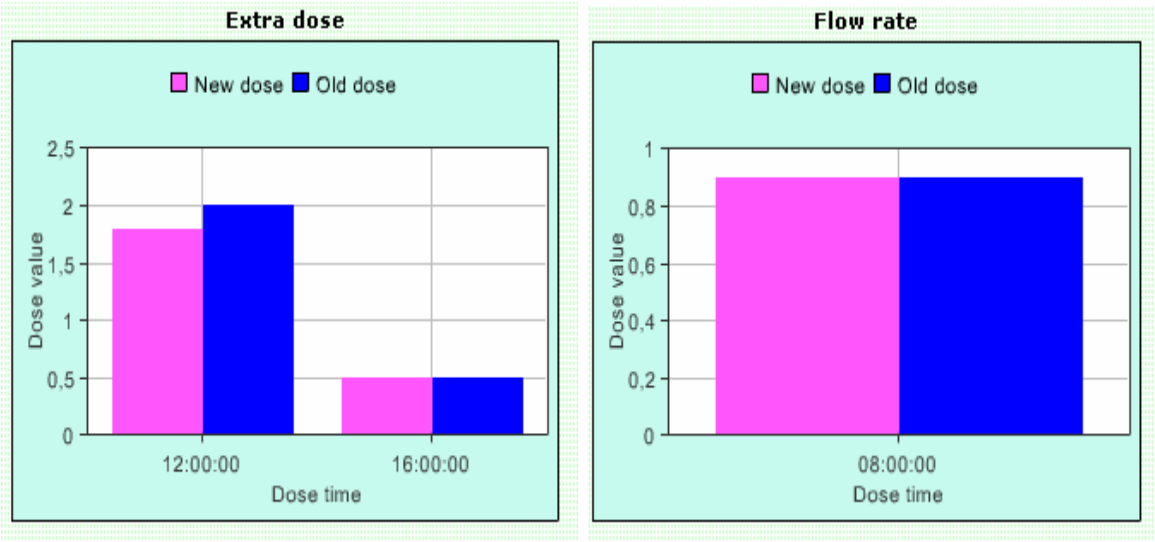


Figure B.1.9: Graphical presentation of advice doses for a patient



FigureB.1.10: Comparison chart between old doses and new doses for a patient (for patient name: BQ and id: 2 in 2004-09-07)

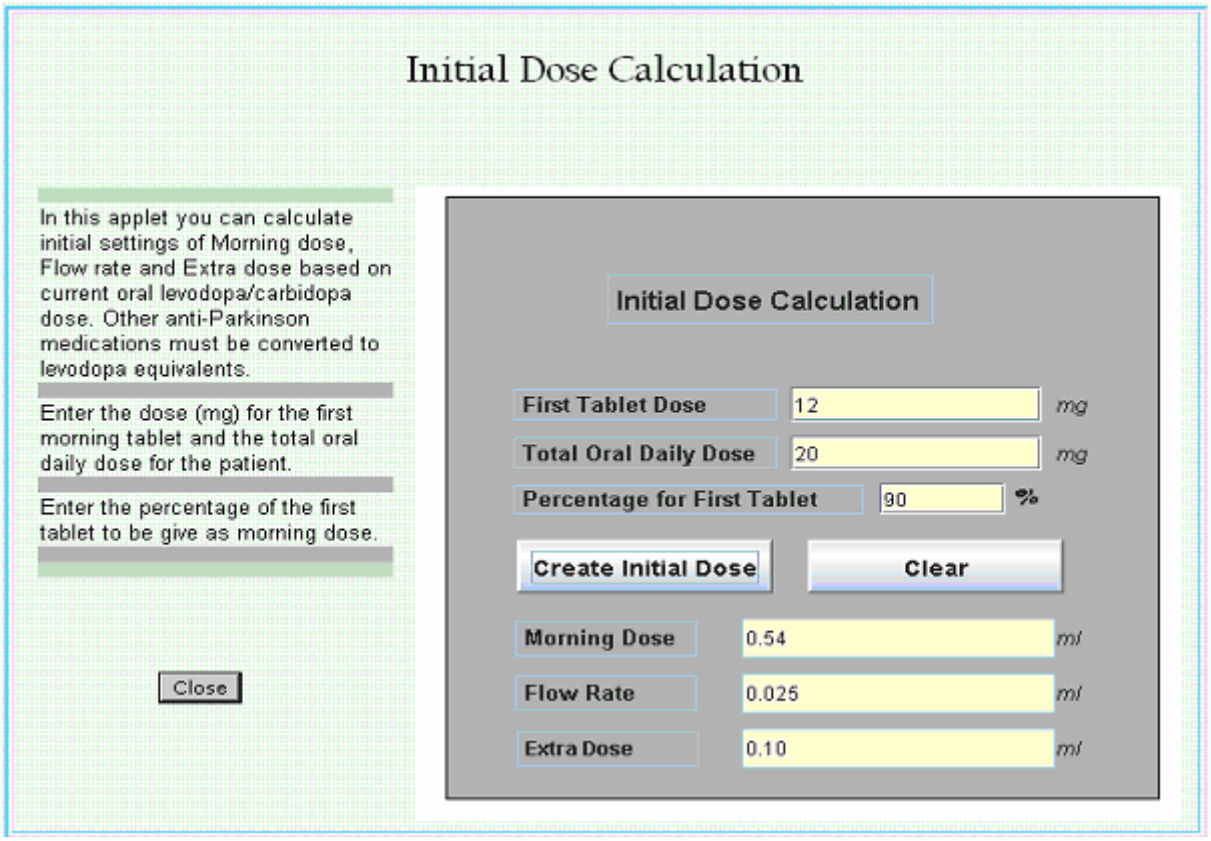


Figure B.1.11: Initial dose calculation page

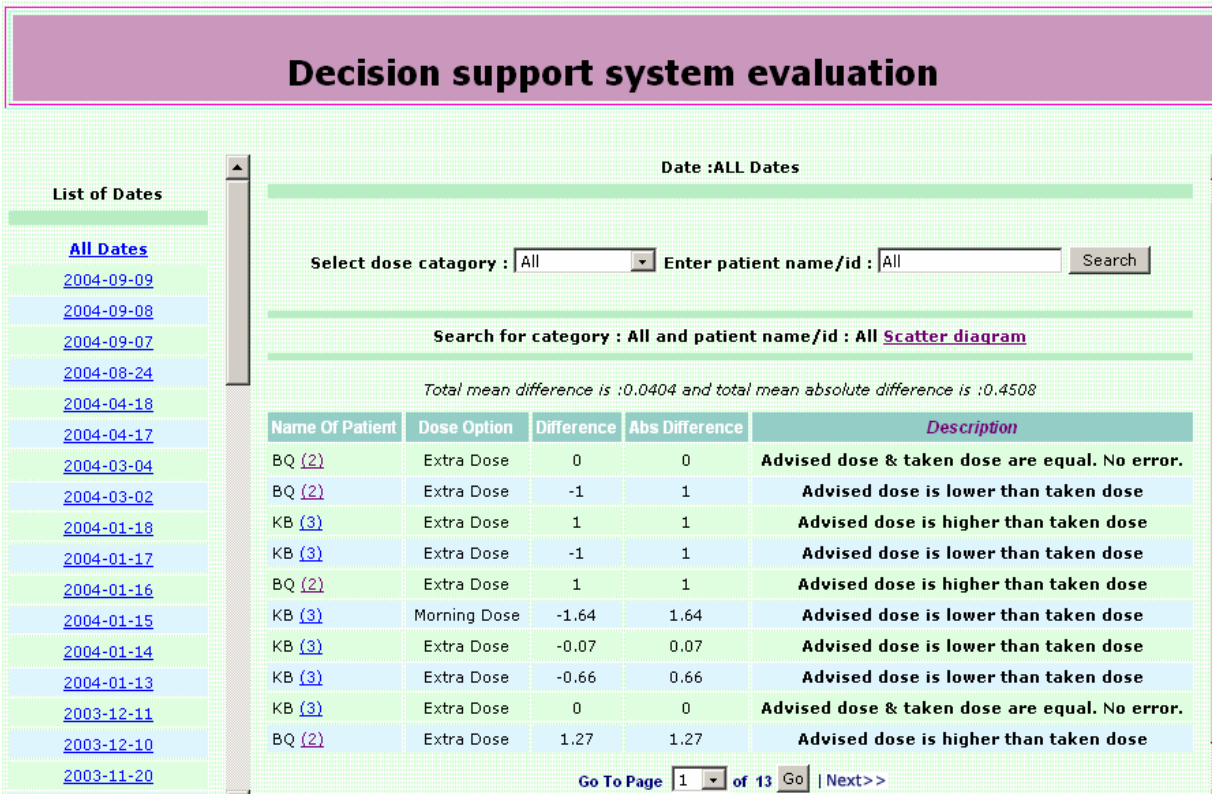


Figure B.1.12: DSS evaluation page

Figure B.1.13: DSS evaluation (Scatter diagram for patient All in All category)

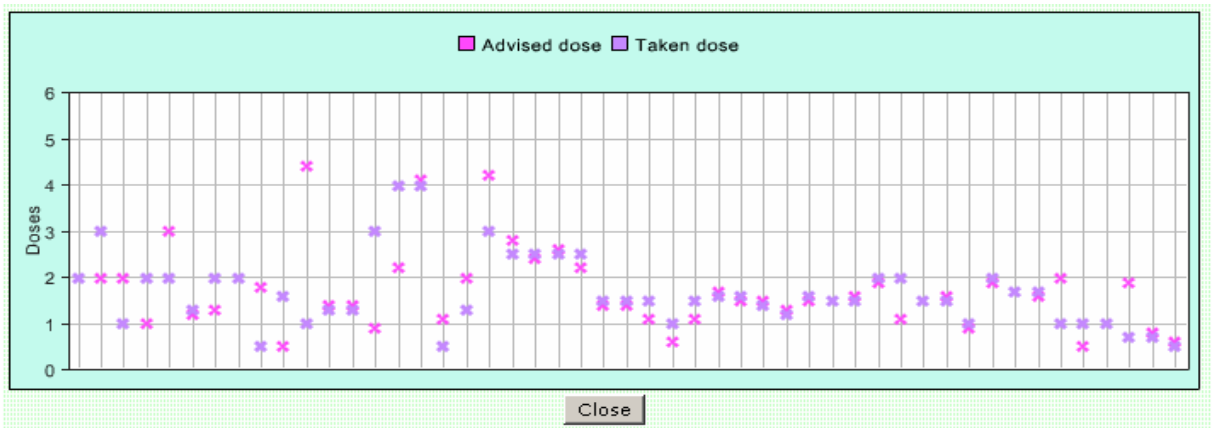


Figure B.1.14: DSS evaluation (Scatter diagram for patient All in Extra Dose category)

Decision support system evaluation for day

Name of patient : BQ and id : 2

Total mean difference is :-0.163 and total mean absolute difference is :0.7584

Dose Date : 2004-09-09

Mean difference is :-0.5 and mean absolute difference is :0.5

Raw data chart — Comparison chart

Dose Option	Advised Dose	Taken Dose	Difference	Abs Difference	Description
Extra Dose	2	2	0.0	0.0	Advised dose & taken dose are equal. No error.
Extra Dose	2	2	0.0	0.0	Advised dose & taken dose are equal. No error.
Extra Dose	2	3	-1.0	1.0	Advised dose is lower than taken dose
Extra Dose	2	3	-1.0	1.0	Advised dose is lower than taken dose

Dose Date : 2004-09-08

Mean difference is :0 and mean absolute difference is :1

Raw data chart — Comparison chart

Dose Option	Advised Dose	Taken Dose	Difference	Abs Difference	Description
Extra Dose	2	3	-1.0	1.0	Advised dose is lower than taken dose
Extra Dose	3	2	1.0	1.0	Advised dose is higher than taken dose
Extra Dose	2	3	-1.0	1.0	Advised dose is lower than taken dose
Extra Dose	3	2	1.0	1.0	Advised dose is higher than taken dose

Figure B.1.15: DSS evaluation for a patient for each day

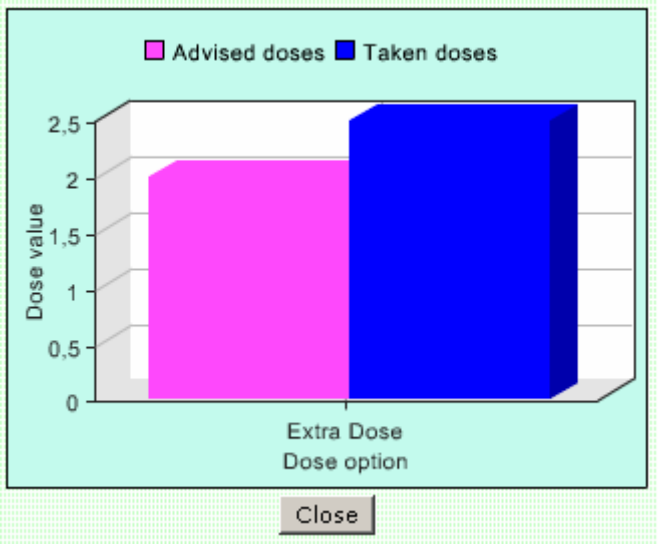


Figure B.1.16: DSS evaluation (Comparison between mean advised doses and mean taken doses for patient name: BQ and id: 2 in 2004-09-09)

Appendix C

C 1 Abbreviation and definition of terms

ANFIS	Adaptive Neuro-fuzzy
CFML	Cold Fusion Markup Language
DSS	Decision Support System
DireQt	Duodopa® infusion - Randomised Efficacy and Quality of life Trial
FIS	Fuzzy logic inference system
FS	Fuzzy set
IDE	Integrated Development Environment
IDOL	Intelligent Dudopa On-Line
MF	Membership function
MV	Membership value
NRC	National Research Council of Canada
PD	Parkinson Disease
RDBMS	Relational database management system
TRS	Treatment response scale

Dyskinesias involuntary movements caused by too much levodopa

Motor fluctuations rapid changes in motor function between off and dyskinetic states.

Goodness-of-fit/R – Square: square of the correlation between the predicted values and the observed values of the dependent variable. Hence, it is an estimate of the proportion of variance in the dependent variable explained by the model. Mathematically, R2 has a lower bound of 0 (although in practice, an R2 exactly equal to 0 is implausible) and an upper bound of 1.0. The larger the value of R2, the better the model predicts the data

Soft Computing is an approach to computing which parallels the remarkable ability of the human mind to reason and learn in an environment of uncertainty and imprecision. (Lotfi A. Zadeh, 1992 [1])

Fuzzy Variable A fuzzy variable defines the language that will be used to discuss a fuzzy concept such as temperature, pressure or height.