Expert system adjudication of hospital data in HIV disease management

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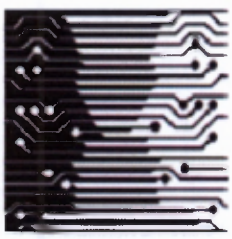

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"I know the meaning of plagiarism and declare that all of the work in thesis, save for that which is properly acknowledged, is my own".

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Abstract

HIV[1] Disease Management Programs (DMP's) are comprehensive programs that are designed to manage the HIV infected patient's treatment in an integrated manner. When an HIV infected patient is hospitalized, the hospital diagnosis may not necessarily be related to their HIV disease (e.g. Insulin-Dependent Diabetes Mellitus). However, because HIV is a progressive immune deficiency disease, it is more probable that the hospital diagnosis is HIV-related. Adjudication of hospital data is critically important for a HIV DMP. This is because key interventions are needed to assess how the hospital diagnosis impacts the patient's HIV disease. The HIV DMP that was investigated in this thesis has a current process during in which a knowledge expert (pharmacist) manually adjudicates hospital data of HIV patients. The adjudication has 2 stages: Stage 1 (plan for intervention which includes various checks and decisions on preliminary action plan) and Stage 2 (actual intervention with the doctor and mutually agreeing on an action plan).

A *HIV-expert system* was developed for the electronic adjudication of hospital data of HIV patients. This expert system uses a pure SQL approach to storing production rules, implementing forward chaining inference and recommending specific actions. The electronic adjudication of hospital data is compared with manual adjudication. The electronic adjudication has the same 2 stages as the manual adjudication, but in the electronic system, the expert system derives the preliminary action plan. Stage 2 in both processes, remains unchanged, as this is the actual intervention with the doctor. For the evaluation of the *HIV-expert system,* a questionnaire was completed by users of the manual system, comparing it with the electronic system.

The main findings are that by implementing the *HIV-expert system* which electronically adjudicates hospital data in an HIV DMP, the time for stage 1 in the electronic system is 53% faster than when the manual system is used. . It was found that the adjudication of hospital data in the manual mode had a 92% accuracy compared with 100% accuracy in automated mode using the *HIV-expert system.* Based on these findings, it can be concluded that the *HIV-expert system does* improve clinical interventions and operational efficiency in an HIV DMP.

[1] See Glossary

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Glossary

Acquired Immunodeficiency Syndrome (AIDS)

A disease of the body's immune system caused by the human immunodeficiency virus (HIV). AIDS is characterized by the death of CD4 cells (an important part of the body's immune system), which leaves the body vulnerable to life-threatening conditions, such as infections and cancers [The Body 2011].

AIDS defining conditions

Any of a list of illnesses that, when occurring in an HIV-infected person, leads to a diagnosis of AIDS, the most serious stage of HIV infection. AIDS is also diagnosed if an HIV-infected person has a CD4 count less than 200 cells/mm^3, whether or not that person has an AIDS-defining condition. The Centers for Disease Control and Prevention (CDC) published a list of AIDS-defining conditions in 1993. The 26 conditions include candidiasis, cytomegalovirus disease, Kaposi's sarcoma (KS), *Mycobacterium avium* complex, *Pneumocystis jiroveci* pneumonia, recurrent pneumonia, progressive multifocal leukoencephalopathy, pulmonary tuberculosis, invasive cervical cancer, and wasting syndrome [The Body 2011].

Aid for Aids (AfA)

An HIV disease management program in South Africa.

Antiretroviral therapy (ART)

The specific medication which an HIV infected patient starts at a specific stage of their disease and adherence/compliance is essential and continued lifelong.

ART is divided into specific classes: Nucleoside Reverse Transcriptase Inhibitors, Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors.

Cytomegalovirus (CMV)

A herpes virus that can cause infections, including pneumonia (infection of the lungs), gastroenteritis (infection of the gastrointestinal tract), encephalitis (inflammation of the brain), or retinitis (infection of the eye), in immunosuppressed people. Although CMV can infect most organs of the body, HIV-infected people are most susceptible to CMV retinitis [The Body 2011].

Disease Management Program (DMP)

Comprehensive programs that are designed to manage specific diseases in an integrated manner.

Human Immunodeficiency Virus (HIV)

The virus that causes Acquired Immunodeficiency Syndrome (AIDS). HIV is in the retrovirus family, and two types have been identified: HIV-1 and HIV-2. HIV-1 is responsible for most HIV infections throughout the world, whereas HIV-2 is found primarily in West Africa [The Body 2011].

Kaposi's sarcoma (KS)

A type of cancer caused by an overgrowth of blood vessels, which causes pink or purple spots or small bumps on the skin. The condition can also occur inside the body, especially inside the intestines, lymph nodes, and lungs. When inside the body, KS can be life threatening. In people infected with HIV, KS is considered an AIDS-defining condition. A virus called Kaposi's Sarcoma herpes virus (KSHV) or human herpes virus 8 (HHV-8) is associated with Kaposi's Sarcoma [The Body 2011].

Opportunistic infections (OI)

An illness caused by any one of various organisms that occur in people with weakened immune systems, including people with HIV/AIDS. OI's that are common in people with AIDS include: Kaposi's Sarcoma, Cytomegalovirus, *Pneumocystis jiroveci* pneumonia (PCP), cryptosporidiosis, histoplasmosis, toxoplasmosis, other infections (parasitic, viral, and fungal) and some types of cancers [The Body 2011]. Kaposi's Sarcoma and Cytomegalovirus which are the 2 conditions discussed in this thesis.

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Chapter 1: Introduction

1.1 The HIV epidemic

The HIV epidemic has a devastating global impact. Recent statistics for people living with HIV indicate that Sub-Saharan Africa continues to bear a disproportionate share of the global HIV burden. This is because an estimated 22.5 million people living with HIV resided in Sub-Saharan Africa in 2009 (representing 68% of the global HIV burden) and about 34% of all people living with HIV resided in the 10 countries of Southern Africa in 2009. With an estimated 5.6 million HIV-positive people, South Africa continues to have the world's largest HIV epidemic [UNAIDS 2010].

Globally, gains continue to be made in the response to the global HIV epidemic. New HIV infections are falling, fewer people are dying of AIDS-related causes and more people with HIV are living longer. Evidence of this is that there were 2.7 million new HIV infections in 2010 (down 21% from the peak of the global epidemic in 1997) and at the end of 2010 an estimated 34 million people were living with HIV worldwide (up 17% from 2001) [UNAIDS 2011].

The positive impact that providing HIV treatment is having can be seen in the following statistics. An estimated 6.6 million people in low and middle income countries were receiving HIV treatment at the end of 2010 (an increase of more than 1.35 million over 2009). As a consequence of expanded treatment, AIDS-related deaths are decreasing, and growing numbers of people with HIV are living longer and productive lives. The number of people dying from AIDS-related causes fell to 1.8 million in 2010 (down from a peak of 2.2 million in the mid-2000s). A total of 2.5 million AIDS-related deaths have been averted since 1995 due to Antiretroviral therapy (ART) being introduced, according to new calculations by UNAIDS [UNAIDS 2011].

1.2 Review of hospital data by an HIV DMP

HIV disease management (DMP) is one of the strategies used in the fight against the HIV epidemic. The core function of an HIV DMP is to increase the access to ART and do the clinical intervention when this is required. From the statistics above, it can be seen that access to treatment does make a significant impact in the fight against HIV. In South Africa, we have huge challenges in this fight and need to use our programs effectively. The HIV DMP needs an integrated approach to HIV disease management and for this reason reviewing hospital data needs to be included in the approach. The use of hospital data in an HIV DMP is standard for reporting and risk analysis purposes. The most important hospital diagnoses that would impact on the patients HIV disease management are outlined below.

1.2.1 Opportunistic infections

Opportunistic infections (OI's) are the specific range of conditions which are the main causes of mortality in HIV infected patients. They are listed as Clinical Stage IV (AIDS) by the WHO [World Health Organization 2007] and as one of the criteria to start Antiretroviral treatment (ART) [SA HIV Clinicians Society 2008]. Numerous studies have shown that the main reasons for hospital admission for HIV patients are various OI's. The intervention by the HIV DMP would be to ensure that the patient is on preventive treatment for the condition, as well as on ART. The intervention also includes checking if the patient requires treatment for the OI condition or the treatment for the OI has a drug interaction with a patient's ART regimen. Should there be a drug interaction, a review needs to be done to check if an amendment in ART dose or regimen is needed. This is to ensure that the ART remains effective. Sub-therapeutic doses will result in drug resistance and ineffective response to therapy

1.2.2 Recurrent hospital admissions for specific conditions

When a patient has recurrent hospital admissions for specific conditions, the intervention by the HIV DMP would be to check if the patient is not adhering to ART. The reason for this is that it has been shown that 80% adherence or greater is associated with lowest death rates [Regensberg et al. 2010].

1.2.3 An adverse drug reaction or toxicity related to ART

When the patient is hospitalized for an adverse drug reaction or toxicity related to ART, the intervention by the HIV DMP would be to review and if necessary change the ART medication.

For these reasons (1.2.1, 1.2.2 and 1.2.3 above), it is clear that adjudication of hospital data is critically important in HIV disease management.

1.3 Objective

In the HIV DMP that was reviewed, hospital data is currently being adjudicated manually by clinical experts. This is both time consuming and is not the most efficient use of highly-skilled resources. This thesis evaluates the electronic adjudication of hospital data for HIV patients using an expert system. An existing adjudication process is analysed, and a rule-based system to automate the process is described along with its evaluation by experts and end-users. Adjudication of hospital data using an expert system is expected to improve clinical interventions. The expert system is named *HIV-expert system*. The focus is on Opportunistic Infection (1.2.1 above) as the hospital diagnosis. The reason for this is the OI's are the leading cause of mortality in HIV patients [Groenewald et al. 2005a] and [Groenewald et al. 2005b; Giarratano et al. 2000; Zwi et al. 2000]

The process followed is that hospital diagnosis and medication information is received and this information is then processed by the *HIV-expert system*. The *HIV-expert system* applies rules which are made up of rule criteria and rule actions. The rule properties are yes/no statements and non-overlapping. The rule criteria are checked and once these are matched for rule, the rule actions are applied to the patient record. This is explained in more detail in future chapters. For a user to review the outcome of rule processing by the *HIV-expert system*, an interface in the form a dynamic website has been developed.

How the process works:

- Hospital diagnosis and medication information received
- Rule processing by the *HIV-expert system*
- Interventionist (pharmacist) checks results of rule processing on the website
- Interventionist contacts the doctor to discuss clinical intervention and agree on an action plan

The *HIV-expert system* will run in the HIV DMP and the users will be interventionist pharmacists.

It is the objective of any thesis to make a contribution to the field which is studied. The main contribution of this thesis is that it is because of the success of the electronic adjudication of pathology results by an HIV DMP, the method was extended to include hospitalization. The electronic adjudication of pathology results by an HIV DMP was presented at 2 separate conferences [van Huyssteen et al. 2003, van Huyssteen et al. 2004]. The first presentation addressed "the need to optimize resource utilisation". The findings was very positive in that "82% required no human action and could be fully processed by the system, and of these, all files monitoring adverse effects were fully automated, 18% of update files required manual intervention and turnaround time reduced from 7-14 days to 1 day" [van Huyssteen et al. 2003]. The second presentation addressed the more complex adjudication of Cd4 & viral load results. The study concluded that electronic adjudication of disease progression and effectiveness of therapy improves operational efficiencies and can be done accurately [van Huyssteen et al. 2004]. The author was fortunate to work on these 2 presentations. The success of that electronic adjudication has to a large extent provided the impetus to extend it to include hospitalization data.

One of the detailed contributions of this thesis is that a prototype website was created in the context of this thesis to evaluate accuracy and performance when the *HIV-expert system* is used by end users. While the user interface is beyond the scope of this thesis, a prototype website was built for users to get an idea of how the details in the *HIV-expert system* can be viewed.

The research methodology used for testing the HIV-expert system was a reiteration of evaluation goals. The evaluation goals are: (1) evaluation of rules, (2) evaluation of rule adjudication for sample of patients and (3) evaluation of rule creation. Qualitative evaluation was done the evaluation of rules and the evaluation of rule creation. Quantitative evaluation was done on the evaluation of rule adjudication for sample of patients.

1.4 Scope

A system to adjudicate hospital data will require a component to import hospital data. The mechanism chosen for data import, and user interface design of an adjudication system, are beyond the scope of this thesis. These aspects are incorporated in the prototype for the sake of completeness only.

1.5 Organization of this thesis

Chapter 2 is a literature review and chapter 3 is an overview of the current adjudication system (EPS). Chapter 4 starts with a high level overview of the HIV-expert system and then continues with details of the system design. Chapter 5 describes implementation of the *HIV-expert system* in SQL and chapter 7 explains how the *HIV-expert system* was evaluated. Chapters 8 and 9 cover the main results and conclusions.

Chapter 2: Background

2.1 Introduction

Automated adjudications of hospital data in an HIV DMP requires an intelligent system and hence falls into the area of Artificial Intelligence (AI). Automated adjudication is only possible because of expertise in this field and because the knowledge can be easily expressed in natural language, hence an expert system is required. Soni notes that: "Assisting physicians in making diagnosis and treatment recommendations is the most commonly found application of expert systems in medical science" [Soni et al. 2011].

This chapter starts with a definition of artificial intelligence and this is followed by the definition of an expert system, its basic structure, the development life cycle, its characteristics which include the advantages and disadvantages of using expert systems. A specific type of expert system is then discussed which is the production rule-based expert system. The last section discusses 2 areas of HIV medicine (clinical conditions in HIV and preventive therapy with co-trimoxazole) which is important for this project.

2.2 Artificial intelligence

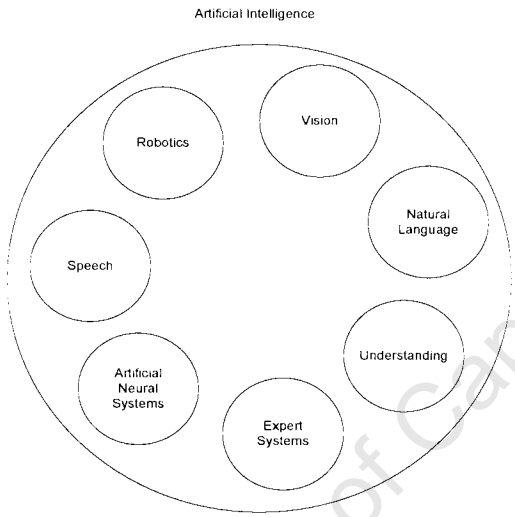
In the Oxford Dictionary of Computing, Artificial intelligence (AI) is defined as: "a discipline concerned with the building of computer programs that performs tasks requiring intelligence when done by humans" [Illingworth 1996]. Within AI, examples of the kinds of tasks which use this are: game playing, automated reasoning, machine learning, natural language understanding, planning, speech understanding and theorem proving. Tasks can be divided into 2 groups: *intellectual* (e.g. game playing and theorem proving) and *perceptual* (e.g. hearing or seeing) [Illingworth 1996]. Expert systems and robotics are areas of AI where computer programs are built to solve problems for technological applications.

Giarratano and Riley [1989] also illustrates that AI has many areas of interest. Figure 1 is from this text. The area of medicine specifically has been significantly impacted by AI applications which have led to the construction of intelligent machines. Expert systems in medicine and the advantages and disadvantages are discussed in more detail in the latter part of this chapter.

The list of primary (and overlapping) areas into which present data artificial intelligence research can be divided broadly was originally listed by Weld [1995] and a summary of each area is provided by Doyle and Dean [1996]. They define the areas as: "(1) knowledge representation and articulation, (2)

learning and adaptation, (3) deliberation, planning, and acting, (4) speech and language processing, (5) image understanding and synthesis, (6) manipulation and locomotion, (7) autonomous agents and robots, (8) multiagent systems, (9) cognitive modelling and (10) mathematical foundations. In the author's view, expert systems fall into the area of "deliberation, planning, and acting". This is because according to Doyle and Dean [1996], this area concerns methods for making decisions, constructing plans or designs to achieve specified goals, and monitoring, interpreting, diagnosing, and correcting the performance of the plans and implementations of the designs.

SOME AREAS OF ARTIFICIAL INTELLIGENCE



Extract from page 2 in GIARRATANO, JC AND RILEY, G. 1989. Expert systems: principles and programming. PWS-Kent, Boston.

Figure 1: Some areas of artificial intelligence

2.3 Expert systems

"A good definition of an expert system is that it is a group of computer programs, along with knowledge, information and databases which act together to simulate the problem-solving and decision-making processes of a human expert within a relatively narrow domain" [Alberico and Micco 1990] . Giarratano and Riley [1989] say "An expert is a person who has expertise in a certain area. That is, the expert has knowledge or special skills that are not known or available to most people." A more technical definition from Hunt [1986] is that an expert system is "computer program that contains both declarative knowledge (facts about objects, events and situations) and procedural knowledge (information about courses of action). Its purpose is to emulate the reasoning process of human experts in a particular domain".

2.4 Basic structure of an expert system

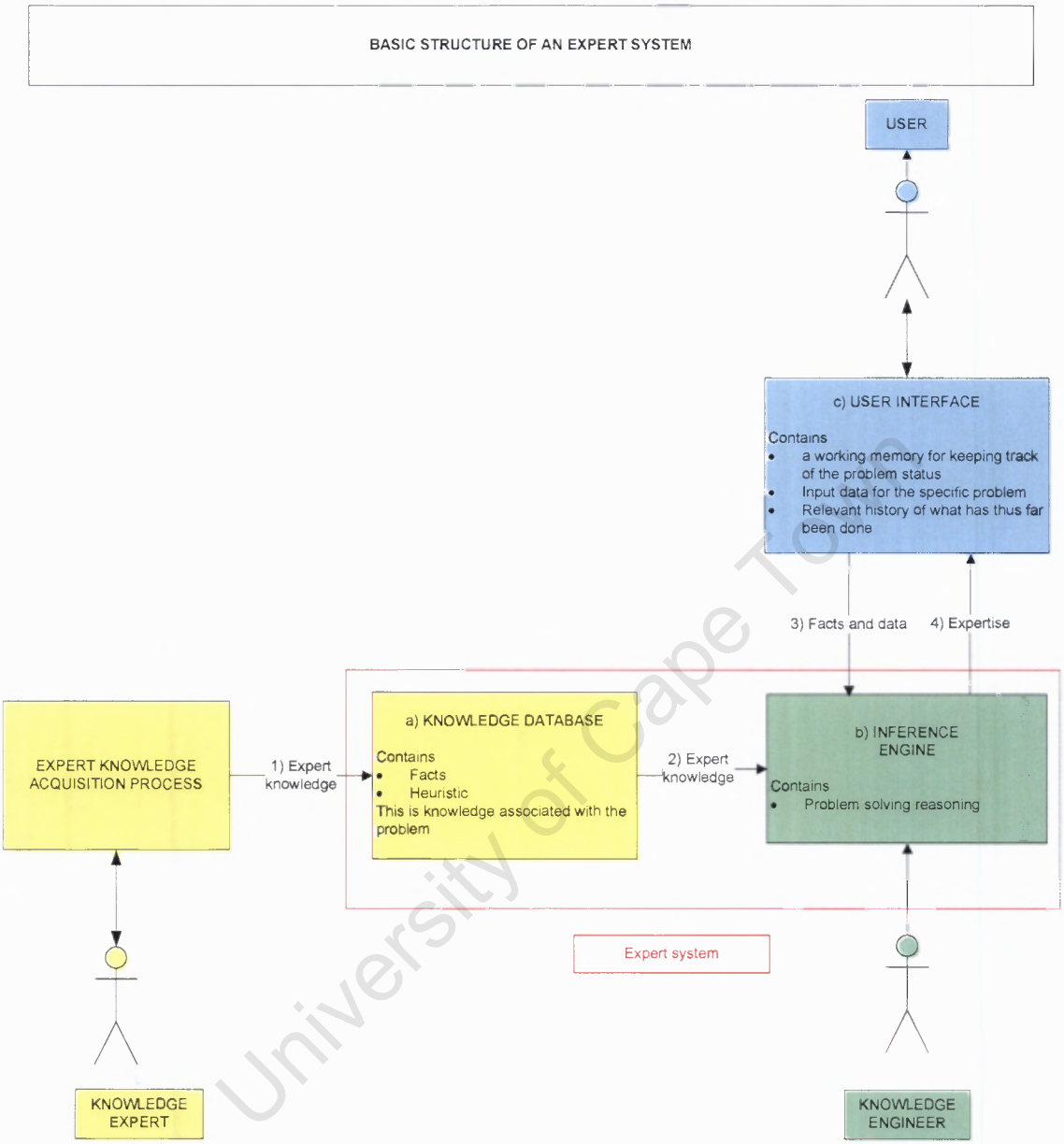
The basic structure of an expert system includes a knowledge base, an inference engine and a user interface [Hunt 1986, Grosan and Abrahams 2011]. *The knowledge database* contains facts and heuristic knowledge. *The inference engine* contains problem solving logic. The *user interface* should be as "natural" as possible by: 1) employing language as close as possible to ordinary language and 2) understanding and displaying images. This is all at speeds that are comfortable and natural to the user [Hunt 1986]. In Figure 2, the basic steps are defined as follows: expert knowledge is used to create the knowledge database, knowledge database passes "expert knowledge" to the inference engine, the user interface passes "facts and data" to the inference engine and the inference engine passes "expertise" back to the user interface.

Hunt explains that facts and heuristic knowledge are collected in a database consisting of information about objects and events on which the knowledge base will work to achieve the desired advice. Some systems use a relational database in which the relationships between objects and events are stored explicitly for flexibility of storage and retrieval [Hunt 1986]. The knowledge base: 1) is used for organizing, controlling, propagating and updating stored knowledge and 2) it initiates searches for knowledge relevant to the line of reasoning upon which the inference system is working. Knowledge is the major factor in the performance of an expert system. This knowledge is in 2 forms: common facts and heuristics. Common facts are knowledge that is widely shared and accepted by professionals in the field. Heuristics are knowledge of good judgement and common practice or "rules of thumb" [Hunt 1986] . A traditional database is "just a database" whereas a knowledge base includes facts, assumptions, beliefs, heuristics, "expertise" and methods of dealing with the database to achieve desired results [Hunt 1986]. Reasoning techniques which manipulate the knowledge are relatively simple. It is the sophistication of the knowledge itself that is important [Ford 1991].

The inference engine: provides a process by which the lines of reasoning are formed; for example, syllogisms and other common ways of reasoning step by step from premises. In the real world knowledge and data are often inexact. Therefore some problem solving inference procedures can use degrees of uncertainty in their inference making.

The knowledge database in an expert system is developed through careful analysis of the knowledge from the "experts" in a field. The most difficult types of knowledge to obtain are: experimental, judgmental knowledge, the knowledge underlying expertise and rules of thumb and heuristic knowledge. Knowledge engineers who study Artificial Intelligence and know how to present knowledge in a computer are needed to: develop the knowledge acquisition process, to create reasoning programs to utilize the knowledge and to assure logical collection of "expert knowledge"

for the creation of an effective knowledge data base. That is called "knowledge engineering" defined as the art of designing and building expert systems and knowledge based programs [Hunt 1986].



Adapted from page 27 in HUNT, V.D. 1986. Artificial intelligence & expert systems sourcebook. Chopman & Hall, New York.

Figure 2: Basic structure of an expert system

According to Black [1986] the traditional life cycle model with the emphasis on the pre-implementations stages of "investigation, analysis, specification and design" describes satisfactorily what needs to be in place in an expert system. The process of building an expert system is called *knowledge engineering* and is done by a *knowledge engineer*. It is interesting to refer to Feigenbaum's [1982] definition: "The knowledge engineer practices the art of bringing the principles and tools of AI research to bear on difficult application problems requiring expert knowledge for their solution. The technical issues of acquiring this knowledge, representing it and using it appropriately to construct and explain lines of reasoning are important problems in the design of knowledge-based system"

Stages in the development of an expert system appear in Giarratano and Riley [1989] as: "(1) the knowledge engineer first establishes a dialog with the human expert in order to elicit the expert's knowledge. This stage is analogous to a system designer in conventional programming discussing the system requirements with a client for whom the program will be constructed. (2) The knowledge engineer then codes the knowledge explicitly in the knowledge base. (3) The expert then evaluates the expert system and gives a critique to the knowledge engineer." This process iterates until the system performance is judged to be satisfactory by the expert.

2.5 Factors affecting the performance of an expert system

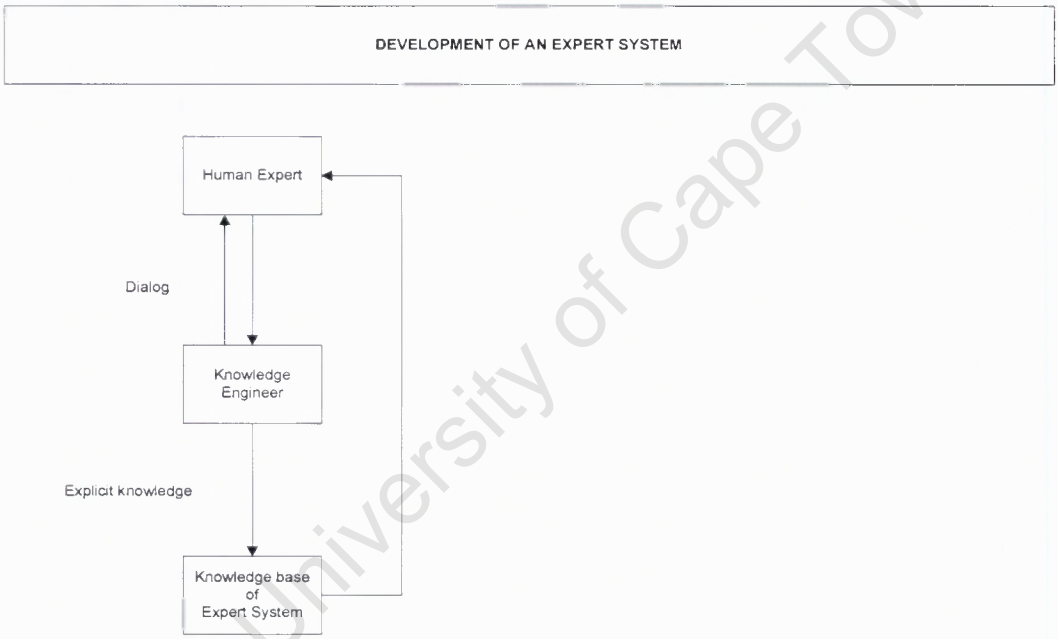
The *pre-requisites* of an expert system are listed by Hunt [1986] as: "there must be at least 1 human expert acknowledged to perform the task well, the primary source of the expert's exceptional performance must be special, the expert must be able to explain the special knowledge and experience and the methods used to apply them to a particular problem, the task must have a well-bounded domain of application". The author is in a fortunate position to be a knowledge expert and the knowledge engineer in the *HIV-expert system*. In this project, the reliability on an additional human expert (first pre-requisite 1 above) is slightly decreased.

Knowledge engineers believe that a good expert system application has these characteristics: it does not require common sense to solve, an expert will need a few minutes to a few hours to solve it and it has an expert committed to system support. Excellent quality advice must be given in a time similar to that required by an expert, or sooner. The system must be reliable, robust and permit adding, changing and removing knowledge [Giarratano and Riley 1989]. Features characterizing an expert system include the abilities to: cope with data which maybe uncertain or partial come to uncertain and where necessary multiple conclusions and explain why it is asking a particular question and how it reached a particular conclusion [Ford 1991].

2.6 Expert system *versus* conventional programming

One important aspect is that the complexity is reduced by focussing the search using rule-based heuristics. The rule-based system is able to reason about its own search effort and reasoning about the problem domain [Hunt 1986].

An expert system differs from conventional programming in the follow respects: an algorithm is used in conventional computing *versus* heuristics and inference used in expert systems; and the separation of knowledge that exists in expert systems. Expert system generally address problems having no algorithmic solution When an algorithm is contrasted with heuristics, an algorithm is defined as a well-understood procedure that is guaranteed to find a solution if it exists or to determine that no solution exists [Hunt 1986].



Extract from page 7 in GIARRATANO, JC. AND RILEY, G. 1989. Expert systems: principles and programming. PWS-Kent, Boston.

Figure 3: Development of an expert system

Heuristics are rules of thumb used by human experts. Many intelligent systems can cope with complex decision making which so far have defied algorithmic systems. These systems often entail uncertain and "fuzzy" data and highly complex chains of reasoning. In other cases, it may be relatively easy to devise an algorithm, but applying the algorithm would take too much time [Ford 1991]. Heuristics (intelligent short cuts) find solution paths without exhaustively trying each possible one. Heuristics are associated with knowledge that is informally defined and empirical, and handles

problems associated with higher levels of uncertainty and imprecision. Algorithms, on the other hand, are associated with knowledge that is highly formalized and completely understood [Ford 1991].

Hunt explains that: "in an expert system, there is separation of the general knowledge regarding the problem from information about the current problem and methods applying the general knowledge to the problem. In a conventional computer program, knowledge pertinent to the problem and methods for utilizing that knowledge is intermixed, so that it is difficult to change the problem. In an expert system, the program itself is only an interpreter for general reasoning mechanisms and the system can be changed by adding or subtracting rules in the knowledge database" [Hunt 1986].

2.7 Expert system advantages and disadvantages

Attractive features of an expert system appear in Table 1 [Giarratano and Riley 1989]. An expert system can make the best knowledge and judgment of many experts widely available in one system.

Feature	Explanation
Increased availability	Expertise is available on any suitable computer hardware.
Reduced cost	The cost of providing expertise per user is greatly lowered.
Reduced danger	Expert systems can be used in environments that might per hazardous for a human.
Performance	The expertise is permanently. Unlike human who may retire, quit or die, the expert system's knowledge will last indefinitely.
Multiple expertise	The knowledge of multiple experts can be made available to work simultaneously and continuously on a problem at any time of the day or night.
Increased reliability	Expert systems increase confidence that the correct decision was made by providing a second opinion to a human expert.
Explanation	The expert system can explicitly explain in detail the reasoning that led to a conclusion. A human maybe too tired, unwilling or unable to do this ALL the time. This increases the confidence that the correct decision is made.
Steady, unemotional and complete response at all times	This may be very important in real-time and emergency situations when a human expert may not operate at peak performance because of stress or fatigue.
Intelligent tutor	The expert system may act as an intelligent tutor by letting the student run sample programs and explaining the system's reasoning
Intelligent database	Expert systems can be used to access a database in an intelligent manner

Table 1: Features of expert systems [Giarratano and Riley 1989]

Giarratano and Riley [1989] indicate that "human experts know the extent of their knowledge and qualify their advice as the problem reaches their limits of ignorance. A human expert also knows when to "break the rules". They propose that "an expert system advice, like a human expert's should degrade gracefully at the boundaries of ignorance instead of abruptly". They add that "expert systems do not have an understanding of the underlying causes and effects in a system. It is much easier to

program expert systems with shallow knowledge based on empirical and heuristic knowledge than deep knowledge based on structure, function and behaviour of objects". Lastly Giarratano and Riley [1989] indicate the repeat cycle of interviewing the expert, constructing a prototype, testing and then interviewing again is very time consuming. Hunt notes some more practical pitfalls are: choosing a poor problem, excessive requirements and inadequate technical and financial resources [Hunt 1986].

2.8 Production rule systems

2.8.1 Knowledge representation in expert systems

There are different ways in which an expert system can represent the knowledge: rule-based systems or production rule system, semantic networks, frames, object orientated programming, reasoning with uncertainty (which includes probabilities such as the Bayesian statistical approach, "fuzzy set" logic and the certainty calculus), case-based systems, neural networks [Ford 1991; Black 1986; Soni et al. 2011]. According to Black [1986], the most popular type of knowledge representation in expert systems "is the production rule notation". In the development of the *HIV-expert system*, the author has used a production rule system.

Systems constructed using rules like "IF...THEN" rules or "production rules" are referred to as rule-based systems [Ford 1991]. The "IF...THEN" is a statement of the relationship among a set of facts. The relationships maybe: definitional (e.g. if female and married then wife) or heuristic (e.g. if cloudy then take an umbrella) [Hunt 1986]. Black [1986] explains that "each rule has 2 essential parts:

(1) *Premise* part (or antecedents) which Soni et al. [2011] calls the condition-part. In principle, it may be an arbitrary Boolean expression, but many expert systems are a little more constrained as an aid to both clarity and implementation.

(2) *Action* part (or conclusion or consequent). In some MYCIN rules for example, alternative conclusions follow from the same premises, each with its own certainty factor."[Black 1986]

Advantages of a rule-based system are: (1) for many problems, humans naturally express their problems solving knowledge in IF...THEN type statements. (2) Since rules are independent pieces of knowledge, they can easily be reviewed and verified. It is modular in nature. This makes it easy to encapsulate knowledge and expand the expert system by means of incremental development. (3) Rules are transparent, and are certainly far more transparent than the modes of knowledge representation employed by neural network [Soni et al. 2011; Giarratano and Riley 1989].

Disadvantages of a rule-based system are: (1) it requires exact matching. If we do not have an exact match, the rule would not work. (2) Rules do not efficiently or naturally capture the representation of complex domain knowledge. (3) Systems with a large set of rules can be slow [Soni et al. 2011].

2.8.2 Inference engine in production rule expert system

According to Black [1986], "an individual rule is said to 'fire' when selected for evaluation. A mechanism is needed for selecting which rules to 'fire' and in which order. This mechanism is called chaining". In a rule-based system, two general methods of inference are *forward chaining* and *backward chaining*. Other methods include means-ends analysis, problem reduction, backtracking, plan-generate-test, hierarchical planning and constraint handling [Giarratano and Riley 1989; Hunt 1986]. The *termination criterion* is a condition that determines that a solution has been found or that none exists. This is necessary to terminate some rule-based systems that find themselves in infinite loops otherwise [Grosan and Abrahams 2011].

Backward chaining

Backward chaining starts from a specification of the desired consequence and proceeds by trying to prove antecedents that will justify concluding the consequent. For this reason, the backward chaining process is called model-directed or goal-directed inference and consequent backward to prove antecedent. Backward chaining is a problem solving method that starts with a goal to be achieved and recursively expands each unsolved goal into simpler sub goals until either a solution is found OR all goals have been expanded into their simplest components [Hunt 1986].

Forward chaining

Forward chaining is a line of reasoning that starts from a known fact and fires rules to infer conclusions. It proceeds from antecedent propositions that are given to whatever consequent propositions are justified. For this reason, the forward chaining process is called data-directed inference and antecedent forward to consequent. The method generates new knowledge until either one of the inferences satisfies a goal or no further inferences can be made. [Hunt 1986].

"Modus ponens" is used in forward chaining. This is shown as

$P \rightarrow Q, P \models Q$ (from P implies Q and the affirmation of P, Q is inferred)

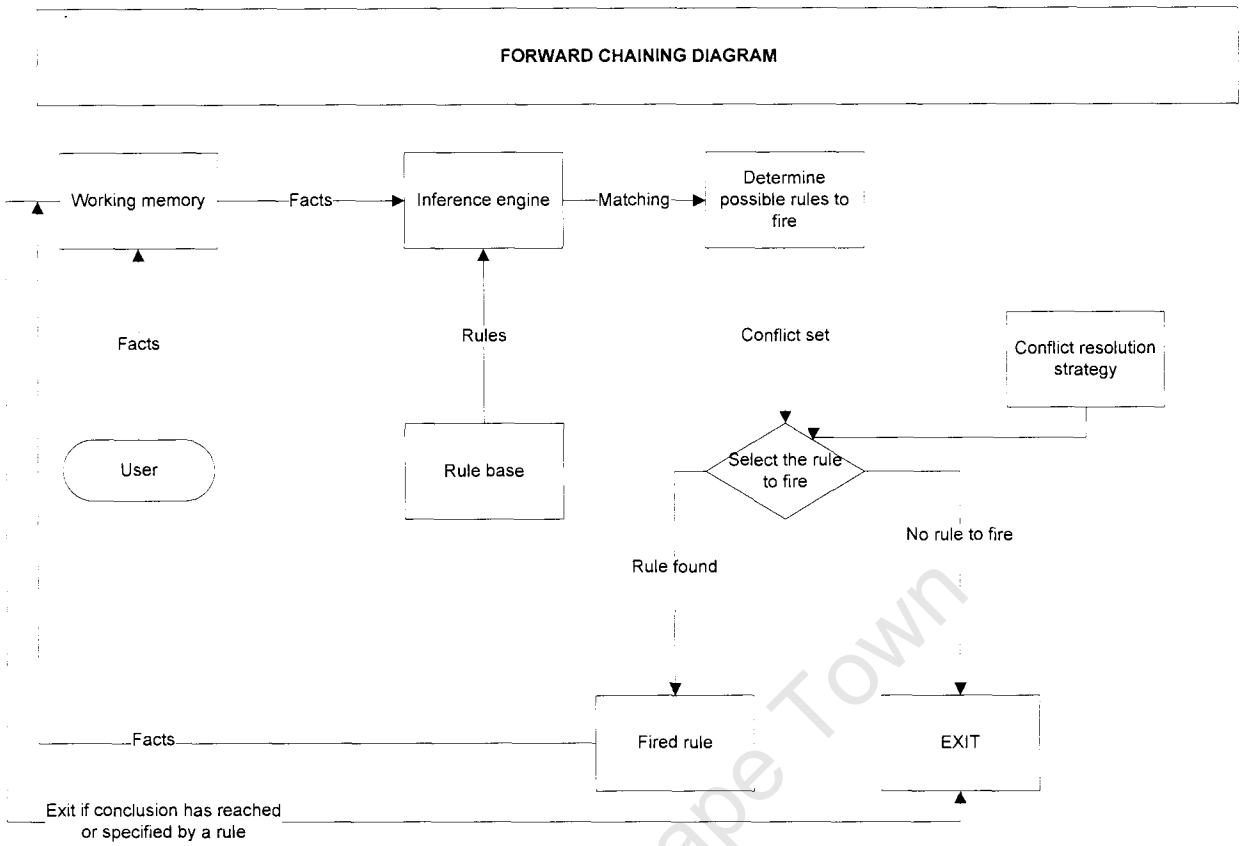


Figure 4: Forward chaining diagram extracted from [Grosan and Abraham 2011]

2.9 Expert systems in medicine

Soni et al. [2011] contains an excellent review of research on expert systems in medicine. They claim these where developed because they: (1) enhance the accuracy of clinical diagnosis through approaches that are systematic, complete, and able to integrate data from diverse sources, (2) increase the reliability of clinical decisions by avoiding unwarranted influences of similar but not identical cases, (3) improve the cost efficiency of tests and therapies, (4) increase our understanding of the structure of medical knowledge, and (5) improve our understanding of clinical decision making, in order to improve medical teaching and to make the system more effective and easier to understand. Some well-known medical expert systems include: INTERNIST, MYCIN, PUFF, QMR and EEG Analysis System [Soni et al. 2011]. According to Giarratano and Riley [1989], MYCIN "showed that AI could be used for practical real-world problems. It was the test bed of new concepts such as the explanation facility, automatic acquisition of knowledge and intelligent tutoring that is found in a number of expert systems today and demonstrated the feasibility of the expert system shell". MYCIN, by explicitly separating the knowledge base from the inference engine, was a milestone in expert system technology because "it meant that the essential core of the expert system could be reused" [Giarratano and Riley 1989].

PUFF was developed in 1979 using the MYCIN shell. Its purpose is to interpret measurements related to respiratory tests and to identify pulmonary disorders [Soni et al. 2011]. INTERNIST continues today under the name CAUCEUS to perform a diagnosis of the majority of disease associated in internal medicine. QMR (Quick Medical Reference) is based on the "massive knowledge base first developed for INTERNIST" [Soni et al. 2011]. EEG Analysis System "was developed for the automated detection of spikes and sharp waves in the EEG for the detection of epileptiform activity" [Soni et al. 2011]

Effective use in clinical practice has been demonstrated in terms of the quality of care, safety and efficiency. "The success of computational intelligence in healthcare is explained by the shift in focus from centering the system on success of the computational performance *versus* the application domain performance" [Bichindaritz and Jain 2010]

2.10 Expert systems in HIV medicine and HIV DMP

The electronic adjudication of pathology results by an HIV DMP was presented at 2 separate conferences [van Huyssteen et al. 2003, van Huyssteen et al. 2004]. The first presentation addressed "the need to optimize resource utilisation". The findings was very positive in that "82% required no human action and could be fully processed by the system, and of these, all files monitoring adverse effects were fully automated, 18% of update files required manual intervention and turnaround time reduced from 7-14 days to 1 day" [van Huyssteen et al. 2003]. The second presentation addressed the more complex adjudication of Cd4 & viral load results. The study concluded that electronic adjudication of disease progression and effectiveness of therapy improves operational efficiencies and can be done accurately [van Huyssteen et al. 2004]. The author was fortunate to work on these 2 presentations. The success of that electronic adjudication has to a large extent provided the impetus to extend it to include hospitalization data.

Lin [1989] created an expert system "for the prevention, diagnosis, detection and recommended treatment for AIDS". The system was rule-based and had the following features: "it contains an antecedents/consequences database and will allow both forward and backward chaining, it has the capability of conflict resolution by context limiting strategy, it is able to explain the deductive and possible inductive process by stepping forward and backward in an Inference Net, it has the facilities to incorporate new knowledge into rules and certainty factors are assigned to the production rules and human experts are consulted to provide empirical transformation function to map input uncertainties onto a certainty of the consequent [Lin 1989]. This covers all aspects from prevention to diagnosis to treatment but the use of hospital data is not covered.

2.11 HIV in medicine

2.11.1 Clinical conditions associated with HIV

There are specific clinical conditions associated with HIV. It was necessary to look at findings on what conditions specifically lead to hospitalization. The spectrum of clinical disease and survival with HIV is different between developed and developing countries. The author will be focusing on research done in developing countries, as this is most relevant to the South African situation.

[Lawn et al. 2008] reviewed mortality rates and causes of death in sub-Saharan Africa and considered possible strategies to address this. The study summarises the key findings such as: key risk factors for early mortality include low Cd4 cell count, advanced clinical stage of disease and the need for patients to pay for treatments; early deaths reflect the spectrum of causes of death prior to ART initiation plus immune reconstitution disease; common causes of death are TB, sepsis, Cryptococcal meningitis, malignancies and wasting syndrome; drug adverse effects are a relatively minor cause of early mortality; strategies to reduce early mortality include screening and management of opportunistic infections.

The study reviewed data in 18 published cohorts. It was interesting to see that even if the data is limited, there is common cause of death across the region. As a HIV DMP in this region we need to review the strategies we use and compare with the ones highlighted in this study. Reducing HIV mortality in general is a core outcome in any HIV DMP and integration of hospitalization data in key in an attempt to achieve this.

[Groenewald et al. 2005a] and [Groenewald et al. 2005b] are retrospective analyses of vital registration data to estimate the "cause specific" mortality rates. Out of potential 22 cause of deaths investigated, 9 were selected for estimating the excess caused by AIDS (TB, pneumonia, diarrhoea, meningitis, other respiratory disease, non-infective gastro-enteritis, other infectious and parasitic diseases, deficiency anaemias, protein energy malnutrition). Specific conditions as "cause of death" gives an indication of what needs to be focused on in the hospitalization data. The conditions listed must form part of the clinical rules in the adjudication system for hospitalization intervention.

2.11.2 Preventive therapy with Co-trimoxazole

Kaposi's Sarcoma and Cytomegalovirus are AIDS defining conditions as per the World Health Organization (WHO) for which co-trimoxazole is used in preventive therapy. The medical term for preventive therapy is prophylaxis and is the term used in this document. The paper "initiating co-

trimoxazole prophylaxis in HIV-infected patients in Africa: an evaluation of the provisional WHO/UNAIDS recommendations" is an observational cohort study of 5 year follow up which had as its objective: to evaluate the proposed WHO/UNAIDS criteria for initiating co-trimoxazole in adult HIV patients in Africa (WHO stage 2-4 or Cd4<500). The study showed survival benefit consistent with previous randomized trials.

This study is interesting because it was as WHO recommendation in 2001 to start co-trimoxazole prophylaxis based on these criteria but this has subsequently change to the new guidelines of co-trimoxazole prophylaxis with Cd4<200 or WHO stage 33 or 4 (irrespective of Cd4 count) [Regensberg et al. 2010]. It gives an indication of how adaptable the rules need to be for changing guidelines. This is an important design consideration that needs to be taken into account.

Other studies include the comprehensive review of preventive treatments across Africa and cover the role of isoniazid and co-trimoxazole [Grant et al. 2001]. Work done in Zambia looked at the role of co-trimoxazole in the prevention of TB [Nunn et al. 2008] and showed that co-trimoxazole is effective is reducing mortality from AIDS defining conditions

2.12 Conclusion

An expert system is "... an intelligent computer program that uses knowledge and inference procedures to solve problems that are difficult enough to require significant human expertise for their solution" [Feigenbaum 2003]. To create an expert system it is necessary to design a knowledge acquisition process, and chose a knowledge representation system and associated reasoning or inference process. To build the expert system requires a knowledge base design, a knowledge engineer capable of obtaining knowledge from experts and encoding it in this structure, an inference engine, suitable user interfaces, and an evaluation system whereby experts can critique and assess the results. The HIV DMP system uses production rules encoded in a relational database and forward chaining inference; its design, implementation and evaluation are described in the following chapters.

Chapter 3: Current adjudication system (EPS)

3.1 Introduction

Before commencing the *HIV-expert system*, a review was done of Aid for Aids (AfA), an HIV disease management program in South Africa. Regular monitoring of Cd4 and Viral Load pathology tests is critically important to identify poor adherence and treatment failure. In addition, the regular monitoring of other specific pathology tests is important to manage toxicity for specific ART. Regular monitoring of patient hospitalizations is also important, because HIV is a progressive disease that affects the immune system. Should the HIV infection remain untreated or inadequately treated, fatality from an AIDS defining condition is inevitable.

Figure 5 shows that HIV DMP staff perform 3 key functions: evaluate clinical criteria, evaluate eligibility for Antiretroviral therapy and interact with the health care professional (doctor) where needed. The current AfA DMP process is as follows: a patient is registered and authorised for medicines (if needed), pathology results are received for the continuous monitoring of disease progression and these results are automatically adjudicated by EPS (an electronic processing system), patient may be hospitalised and currently this is adjudicated manually by clinical experts and after adjudication the doctor is consulted to discuss an action plan. In this thesis, the author has developed an *HIV-expert system* for the electronic adjudication of hospital data. The combination of pathology and hospitalization adjudication by electronic means aims to improve clinical efficiency.

3.2 Different levels of skill in an HIV DMP

In a HIV DMP, there are different levels of skill among staff. For the adjudication of hospital data, a clinical expert is needed to evaluate the patient record. They will do a review of all the information (patient's clinical status, stage of disease, ART medication and hospital diagnosis information and treatment for that diagnosis), plan the intervention and then do the actual intervention with the doctor. There are usually 2 levels of intervention. Level 1 is a high priority intervention which is done by a pharmacist. A detailed interaction with the doctor needs to take place discussing which ART medicines will be best for this patient taking into account their hospitalization details, HIV pathology results, co-existing conditions etc. Level 2 is a lower priority intervention which is done by a pharmacist assistant. This level is for the cases where the patient needs to be on prophylaxis and chemotherapy but is already on ART, so a less detailed interaction with the doctor needs to take place. This tiered priority intervention structure ensures that the correct level of expertise is focussed on the correct areas. The high priority interventions are done by experienced clinical staff.

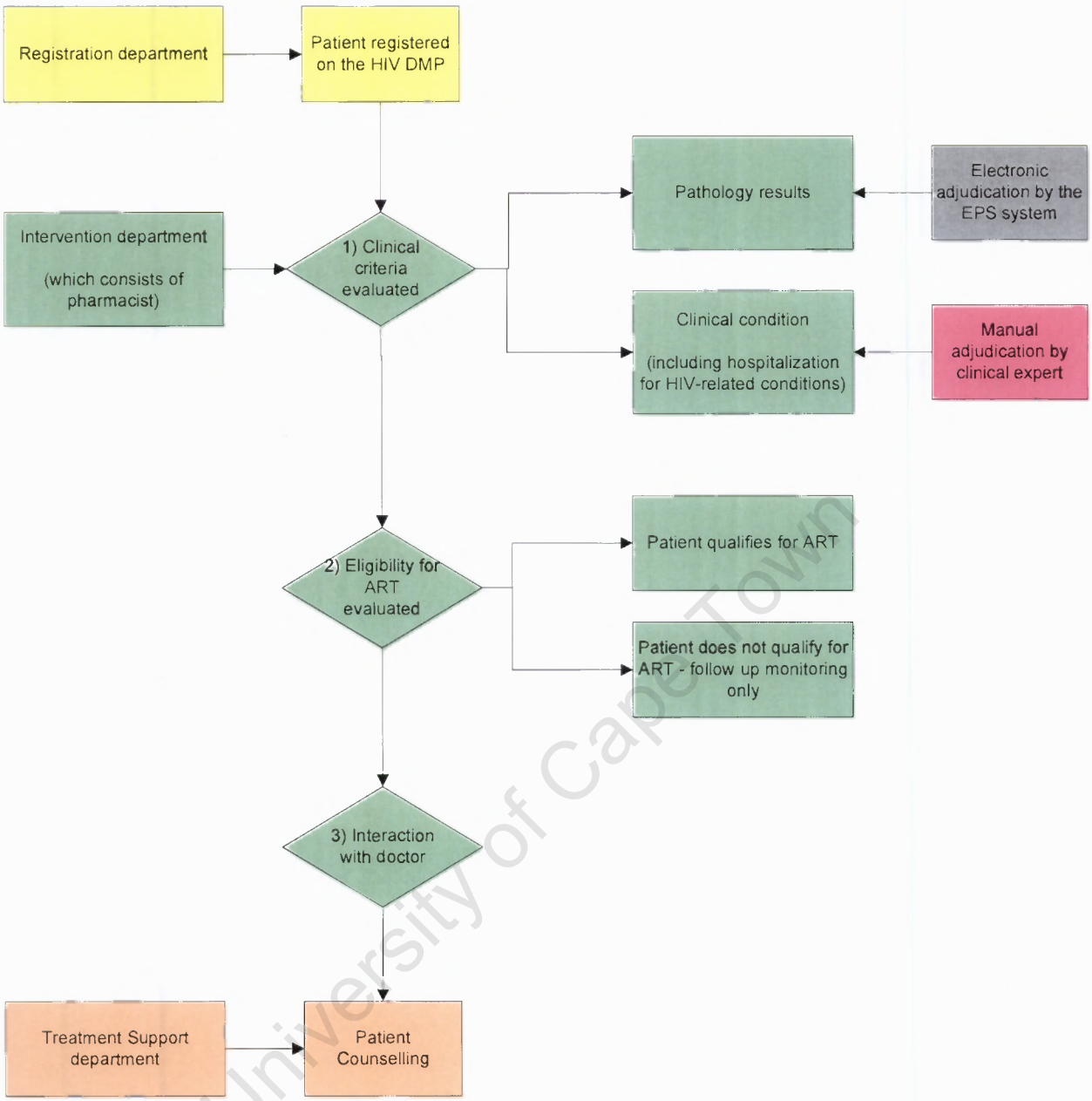


Figure 5: Overview of operations department in an HIV DMP

3.3 Current manual adjudication for hospital data

When information is received that a patient is hospitalized, this is manually adjudicated by clinical expert. This means they need use their expert knowledge to review the hospital diagnosis by checking if it is related to the HIV condition. If it is not related to HIV, for example Insulin-Dependent Diabetes Mellitus, no further intervention action is needed. However, if it is related to HIV, for

example Kaposi's Sarcoma, the further intervention is needed. This mainly includes checking if the patient is on Anti-retroviral therapy, preventive therapy for specific HIV related conditions and therapy for the specific hospital diagnosis.

This process of manual adjudication is critical but also time consuming and not the most efficient use of expert knowledge. A system that can electronic adjudicate hospital data would be beneficial because the system can: filter out the hospital diagnosis not related to HIV, check for which therapy the patient is on, pass only the non-routine or "problem" files for intervention action and assist the intervention staff with an action plan to be discussed with the doctor.

3.4 Current system adjudication for pathology results

Monitoring updated pathology results for patients on the program is a key component of the AfA program. This was initially done manually, but EPS was subsequently introduced to adjudicate pathology results. EPS will determine if the applications meet: (1) "routine" criteria i.e. system assigns the follow up and no manual user intervention occurs or (2) "intervention" criteria i.e. system routes the file to a clinical expert to review and intervene on. The intervention in most cases involves contacting the doctor and agreeing on an action plan for that patient.

The existing EPS system is restricted to pathology results, and is made up of 3 main sub-processes

a) Pre-screening

This sub-process runs each morning at 3am. It then identifies new applications for screening. When a new pathology result has been captured, this is the trigger that the pre-screening sub-process uses to move the file to electronic screening.

b) Manual cancellation of electronic screening

This sub-process runs when a user manually selects "cancel electronic screening". This marks off the unprocessed results as having been processed by electronic screening.

c) Electronic Screening

This sub-process runs every 15 minutes between 5am and 6pm daily. It processes the pathology result to mark/flag the application as urgent where the result is within the "urgent" range; and to indicate specific actions where necessary according to the range within which the value falls [Foster 2010].

3.4.1 Prescreening

In the current system which does the adjudication of pathology results, all pathology results that have been captured are assigned an Electronic Processing Code (EPC) of 0. EPC is an internal coding

system that used in the electronic screening process. The EPC is updated to any value from 1-5 depending on the outcome of pre-screening or electronic screening.

EPC code	Description
0	Not processing by electronic screening
1	Electronic screening complete
2	File for screening
3	File for intervention
4	File for counselling
5	Electronic screening cancelled – manual override by user

Table 2: EPC Codes in EPS system

3.4.2 Electronic Screening

In the current system which does the adjudication of pathology results, the electronic screening process starts off getting the list of applications. It then gets a list of electronic screening rules to check the applications against. Next, it gets a list of criteria which make up the rule being processed and captures a note on the application. After that it executes the "process rule criteria" stored procedure. Once all the rule criteria are passed, it executes the "apply rule actions" stored procedure. Once all the rules have been checked, the system then the EPC. Figure 7 which is the activity diagram showing the electronic screening rules [Foster 2010].

The key benefits of EPS [van Huyssteen, et al. 2004] were that: (1) it reduced the turn-around time for "routine" criteria applications by no longer having to wait for users to intervene, (2) ensured the accuracy of follow up date assignment as this is no longer subject to user error, (3) ensured that the files that meet the "intervention" criteria are reviewed ahead of files that meet the "routine" criteria and (4) most importantly clinical staff are then able to focus their attention on the applications for "intervention". This was the result presented in the first presentation on the EPS data on Cd4 & Viral Load pathology results at the HELINA conference [van Huyssteen et al. 2003] .This was followed by additional data presented at the IAS conference which looked at the EPS process for different pathology results [van Huyssteen, et al. 2004]. This project aims to extend these benefits to the processing of hospitalization data, by constructing an expert system to categorise such cases as "routine" or "non-routine", and to indicate the required actions to take, with an explanation for each.

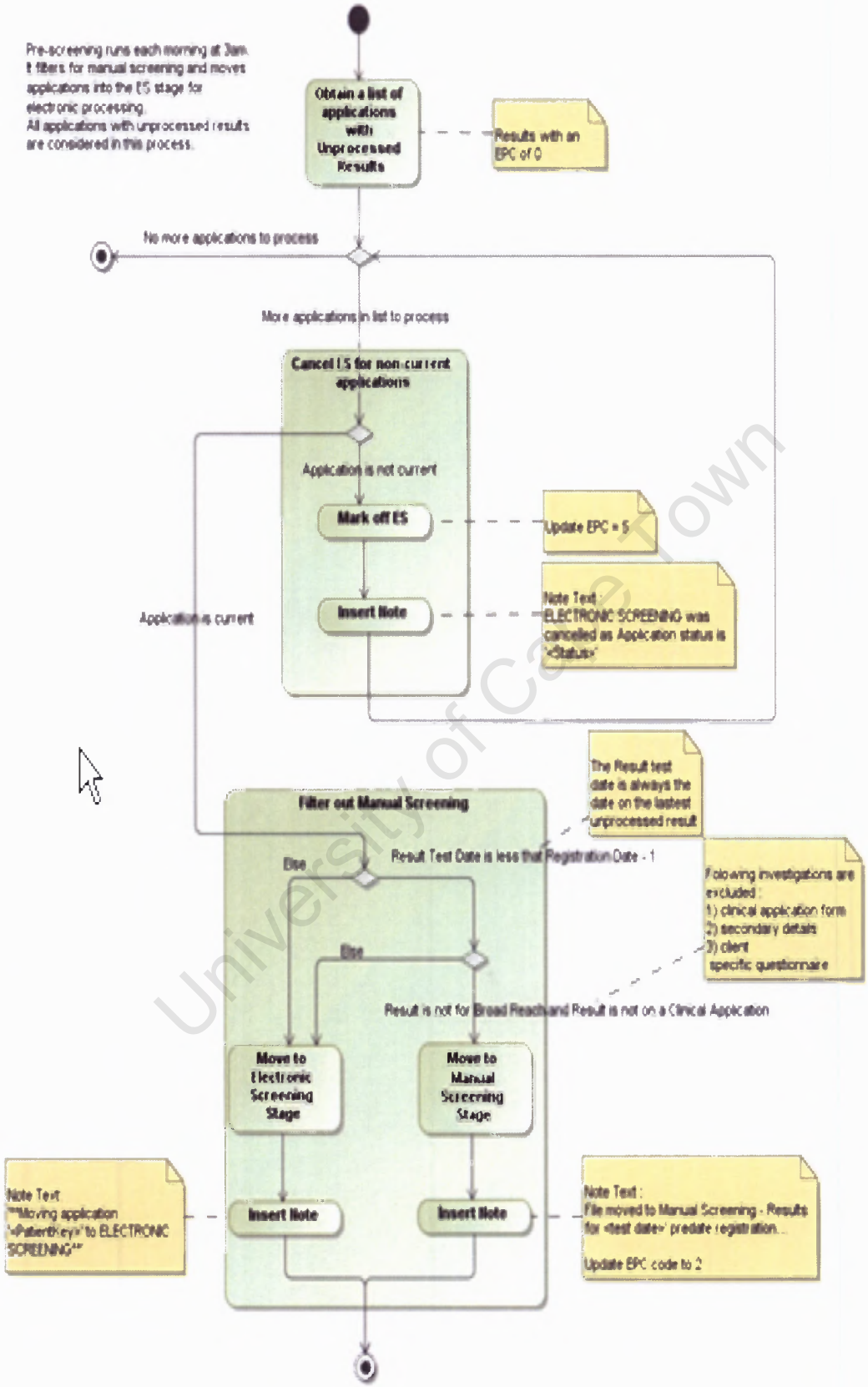


Figure 6: Activity diagram for the prescreening process in EPS [Foster 2010]

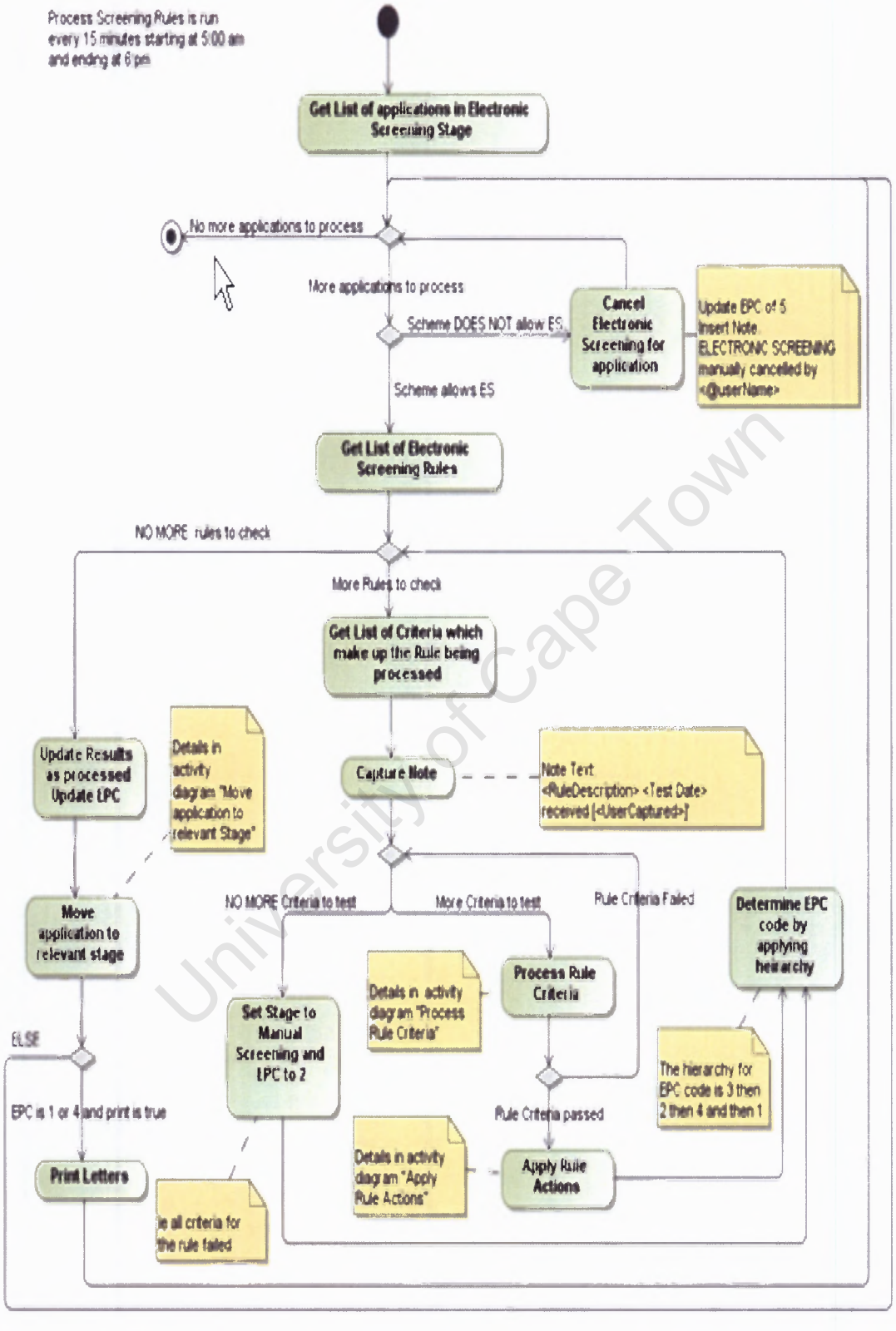


Figure 7: Activity diagram for the electronic process in EPS [Foster 2010]

3.5 Concluding remarks

Clinical criteria that need to be evaluated are classified into 2 groups: pathology results and clinical conditions which include hospitalization related to a HIV condition. At present, humans adjudicate hospital data and the EPS system adjudicates pathology results in an HIV DMP to monitor disease progression and effectiveness of therapy. By using the EPS system it was reported that 82% of the files were fully or partially processed by this system and turnaround time dropped from 7-14 days to 1 day [van Huyssteen et al. 2003]. This data was followed up with similar results for different tests in [van Huyssteen, et al. 2004].

The success of the current EPS is one of the main reasons the new system (*HIV-expert system*) was developed. The current system does the adjudication of pathology results while the new system (*HIV-expert system*) applies to the more complex process of electronic adjudication of hospital data. While the current system derives actions and categorisations by checking in which pre-defined range a pathology result falls, the hospital data adjudication requires applying a complex system of rules, as explained in the next chapter.

Chapter 4: *HIV-expert system* overview and design

4.1 Introduction

The chapter starts off with an overview 4 core components of the system. Next, the evaluation of the system is described and evaluation goals are listed.

4.2 System components

The *HIV-expert system* consists of 4 main processes: receive patient diagnosis data from hospital, receive patient medication data from HIV DMP, check rule criteria in *HIV-expert system* and process rule actions in *HIV-expert system.*

The system components are:

(1) An interface to external systems. External systems include: rules created by expert, diagnosis data from hospital and medication data from HIV DMP

(2) *HIV-expert system* database. This contains the knowledge base used to implement the electronic adjudication. It contains all the tables and stored procedures needed for rule processing

(3) Rule processing by expert system. This takes the data received from external systems and applies the expert rules for electronic adjudication.

(4) Interface for end user. This is an interface that is used by an end user to review the recommendation from the *HIV-expert system* from the rule adjudication.

See Figure 8 for an illustration of the system components.

4.3 Hospital data adjudication system overview

As outlined in chapter 2, expert system creation requires the design of a knowledge acquisition process, knowledge base and inference engine; as well as a mechanism for evaluating results. It also requires an appropriate user interface, which is not within the scope of this project and is left for future work.

The *HIV-expert system* uses production rules, and the knowledge specific to the problem domain is separate to the procedure that manipulates it (inference). The inference method used is forward chaining because proceeds from the antecedent (e.g. hospital diagnosis) to the consequent (e.g. intervention action). A relational database was chosen for the knowledge base because of its reliability, efficiency and extensibility. Knowledge acquisition involved the author, herself a pharmacist at AfA acting as knowledge engineer – choosing an appropriate set of rules for the prototype, designing a database schema and inference mechanism, and encoding and testing these

rules. Thereafter other experts were given simple user interfaces for adjudicating hospital data and for entering new rules, and finally the system evaluation was designed for testing accuracy and performance.

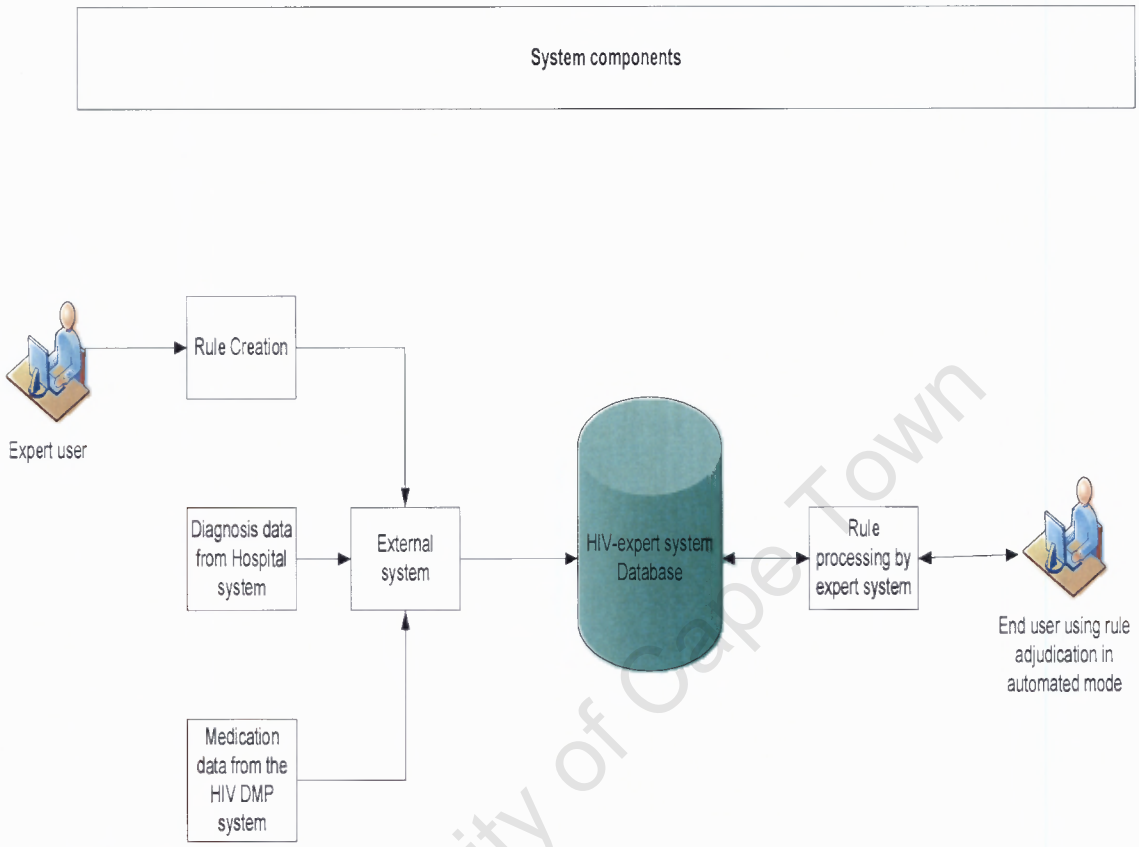


Figure 8: Diagram of system components

4.4 Evaluation goals

For the *HIV-expert system* developed in this thesis, the evaluation goals are:

1. Evaluation of rules
    - Is the rule set up correct for existing rules? Prior to implementation, does a clinical expert need to check the rules to be applied by the expert system? Post implementation, does a "human" user need to check each record processed by the rules in the expert system?
2. Evaluation of rule adjudication for sample of patients
    - Is adjudication in automated mode correct for a sample of patients (20 patients)?
    - Is adjudication in automated mode faster than manual mode for a sample of patient (20 patients)?
    - Is adjudication in automated mode more accurate than adjudication in manual mode for a sample of patient (20 patients)?

- Would the rule adjudication be used with confidence on real patients? Does it improve clinical intervention?

3. Evaluation of rule creation

- Is the new rule creation spreadsheet usable?
- Is adjudication using the new rule correct for a sample of patients?
- Is the new rule creation process usable?

Alignment of the rules to the treatment principles for specific diagnoses: Kaposi's Sarcoma and Cytomegalovirus was checked by expert users. Feedback was in the form of survey questions, and was also done for new rules entered by AfA experts. Comparison of the same patient records adjudicated in manual mode and automated mode was done based on time taken and accuracy as assessed by experts. A new rule was captured by expert users and then loaded into the system. A questionnaire was then answered to check the usability of rule entry. Feedback is in the form of survey questions.

4.5 HIV-expert system design

This chapter gives an overview of how the *HIV-expert system* for the adjudication of hospital data in HIV disease management was designed and the details of the design.
The chapter starts off with explanation of how an HIV DMP operates. This is the context in which the *HIV-expert system* was developed. It is important to understand some of this background when analysing the system design. Next, the logical process of setting up a rule in the system is explained. The first step is to select the rules to be designed. Once Kaposi's sarcoma and Cytomegalovirus were selected, the treatment principles of these clinical conditions were reviewed. The next step followed was to implement the treatment principles into actual rule design. In an attempt to best explain the rule design, first the rule process flow is listed and this is followed by a simplified rule diagram. In chapter 6, a more detailed version of the rule diagram is explained.

4.6 Rule properties

The rule properties are rule criteria and rule actions. Rule criteria include: checking the hospital diagnosis, checking if the patient is on ART, checking if the patient is on Co-trimoxazole Prophylaxis and checking if the patient is on Chemotherapy or Antivirals. Rule actions include: add note, update EPC, update stage and update priority. The rule criteria and rule action are specified based on the treatment principles for that specific rule.

Each OI has a range of possible variations with each specific variation making up a specific rule. A rule set is made up a range of branches for that specific diagnosis. This is best illustrated by the example:

- Rule set = Kaposi's Sarcoma
- Rules = Kaposi's Sarcoma Rule 1 to Rule 8
- Each rule has specific rule criteria and rule actions

4.7 Rule design for Kaposi's Sarcoma (KS)

4.7.1 Treatment principles for Kaposi's Sarcoma

Kaposi's Sarcoma (KS) is defined in the Handbook on HIV medicine as follows:

> It is a multifocal neoplastic proliferation of endothelial cells. It presents as one or more reddish or slightly bluish swellings with or without ulceration. It presents with multifocal vascular plaques or nodules in the skin or viscera. KS-associated herpes virus has been identified in all forms of KS. Lesions can occur in any location, but are usually multiple and occur frequently on the face, oral mucous membranes and lower extremities. Oral lesions occur commonly on the hard palate. Intraoral lesions are initially asymptomatic, but as they progress, patients may have associated pain associated with ulceration, bleeding and super infection. In the disseminated form, the lymph nodes, lung and gastrointestinal tract are commonly involved. Bilateral lower-lobe infiltration and pleural effusions are common in pulmonary KS. KS follows a variable clinical course ranging from indolent skin plaques to aggressive malignancy with early visceral involvement but, ultimately is a progressive disease in all its forms. A biopsy is essential for a definitive diagnosis. KS can occur at any CD4 but is more aggressive at low counts. Without Antiretroviral therapy, the disease is progressive. Treatment decisions are made on the basis of the extent of the disease. For isolated oral lesions, local therapy may include laser or surgical excision, radiation or intralesional chemotherapeutic injections. Systemic chemotherapy is usually indicated in patients with widespread progressive disease [Wilson 2008].

What can be summarised from the above is the clinical presentation of KS which ranges from nodules in the skin or mouth to full systemic (entire body) involvement. Patients with KS must be on ART because the disease is progressive without this. If the lesion is local, treatment with systemic chemotherapy may not be needed.

This is reiterated in the AfA[2] clinical guidelines [Regensberg et al. 2010]. The treatment principles for Kaposi's Sarcoma (KS) are summarised as: (a) all HIV-positive patients with KS should be commenced on ART as KS is a Stage 4 AIDS defining condition and ART prolongs the time to treatment failure on KS chemotherapy, (b) Co-trimoxazole prophylaxis should be commenced given that this is a Stage 4 AIDS defining condition [World Health Organization 2007], (c) KS chemotherapy may not be required for all patients with KS (many patients with limited mucutaneous KS will have complete resolution or substantial regression on ART only), (d) KS chemotherapy may be required for patients with KS.

KS chemotherapy[3] medication include: Vinca alkaloids (Vincristine and Vinblastine), Taxanes (Paclitaxel), Anthracyclines (Doxorubicin and Daunorubicin) and other antibiotics (Bleomycin) [Gibbon et al. 2000]. The most important drug interactions between KS chemotherapy and ART are: (1) Zidovudine[4] combined with all chemotherapy has as increased risk of myleosuppression (bone marrow suppression), (2) Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)[5] may reduce the levels of paclitaxel and vincristine/vinblastine and (3) Protease Inhibitors (PI's)[6] may increase the levels of these agents.

4.7.2 Implementation of treatment principles for Kaposi's Sarcoma

Based on the treatment principles, the author defined the rule criteria and rule action to be applied by the *HIV-expert system*. For the Kaposi's Sarcoma rule set to apply the patient needs to have KS as a hospital diagnosis. This is referred to as the "entry" criterion for rule check. Note: In the rule diagram that follows, rule criteria are colour coded yellow while the rule actions are green. See Table 3 which summarises the rule criteria and rule actions for Kaposi's Sarcoma.

[2] Aid for Aids is a HIV disease management program in South Africa

[3] KS chemotherapy is a specific is a specific group of medication used to treat KS. It is made up of various classes. For example Vinca alkaloids is a class of which Vincristine and Vincristine are examples

[4] Zidovudine is in the Nucleoside Reverse Transcriptase Inhibitors class of ART medication

[5] Non-Nucleoside Reverse Transcriptase Inhibitors is a class of ART medication

[6] Protease Inhibitors is a class of ART medication

Rule Criteria		Rule action	
Description	**Reason**	**Description**	**Reason**
Patient needs to have a hospital diagnosis = Kaposi's Sarcoma	"Entry" criteria for rule check		
Patient needs to be on medication = ART	Treatment principle a)	Level 1 intervention	Detailed discussion with Dr is needed
Patient needs to be on medication = Co-trimoxazole prophylaxis	Treatment principle b)	Level 2 intervention	Less detailed discussion with Dr is needed
Patient maybe on medication = chemotherapy for the treatment of Kaposi's Sarcoma	Treatment principle d)	Level 1 intervention	Detailed discussion with Dr is needed

Table 3: Summary of rule criteria and rule actions for Kaposi's Sarcoma

4.7.3 Rule diagram process flow for Kaposi's Sarcoma

See Figure 9 for an illustration of the rules (simplified rule diagram for Kaposi's Sarcoma). There are 8 rules which make up the Kaposi's Sarcoma set of rules. The process flow is numbered in sequence and the sequence is critical for manual human adjudication. The *HIV-expert system* has been designed to mimic this sequence for ease of successful implementation. The rule starts off by checking if the patient is diagnosed with hospital diagnosis of Kaposi's Sarcoma. The next a check is if the patient is on ART (this is the first medication check. It has been placed above other medication check because the treatment principle listed above is critical). After this, the check is done if the patient is on Co-trimoxazole Prophylaxis for each branch of: (1) "Patient NOT on ART" and (2) "Patient on ART". Lastly a check is done if the patient is on Chemotherapy for the treatment of KS for each branch of: (1) "Patient NOT on ART" and "Patient NOT on Co-trimoxazole Prophylaxis", (2) "Patient NOT on ART" and "Patient on Co-trimoxazole Prophylaxis", (3) "Patient on ART" and "Patient NOT on Co-trimoxazole Prophylaxis" and (4) "Patient on ART" and "Patient on Co-trimoxazole Prophylaxis".

4.8 Rule design for Cytomegalovirus (CMV)

4.8.1 Treatment principles for Cytomegalovirus

According to the John Hopkins Medical Management of HIV infection, the different types of Cytomegalovirus (CMV) infections are: CMV retinitis, CMV oesophagitis or colitis, CMV encephalitis and CMV pneumonitis [Bartlett and Gallant 2004]. Cytomegalovirus retinitis is defined in the Handbook on HIV medicine as follows:

> It is the most common cause of visual loss, even in Africa where the incidence is lower than in the developed world. It presents when the Cd4 count ranges between 100 and 50 cells/ul.

Bilateral disease is found in 20% to 40% of patients. The natural history of CMV retinitis is that if untreated, it is relentlessly progressive and destroys the whole retina within 6 months. Ideal treatment therapy of CVM retinitis is systemic induction therapy followed by maintenance therapy with either intravenous Ganciclovir or oral Valganciclovir [Bartlett and Gallant 2004].

What can be summarised from the above is the clinical presentation of CMV which is most common in the keys but can spread to the gastrointestinal are and nervous system. As with KS, it is progressive disease so that patients must be on ART because the disease is progressive without this. Therapy with an Antiviral is essential.

Again this is reiterated in the AfA clinical guidelines [Regensberg et al. 2010]. The treatment principles for Cytomegalovirus (CMV) are summarised as: (a) all HIV-positive patients with CMV should be commenced on ART as KS is a Stage 4 AIDS defining condition (early initiation of ART approximately 2 weeks is essential in all cases, (b) Co-trimoxazole prophylaxis should be commenced given that this is a Stage 4 AIDS defining condition [World Health Organization 2007] and (3) CMV antiviral therapy is needed for all patients with CMV antiviral therapy[7] medication include: Ganciclovir and Valganciclovir.[Gibbon et al. 2000] The most important drug interactions between CMV antiviral therapy and ART are: Zidovudine is best avoided in combination with Ganciclovir or Valganciclovir as both agents cause myleosuppression (bone marrow suppression).

[7] CMV antiviral therapy is a specific group of medication used to treat CMV. It is made up of Ganciclovir and Valganciclovir

4.8.2 Rule diagram for Kaposi's Sarcoma - simplified

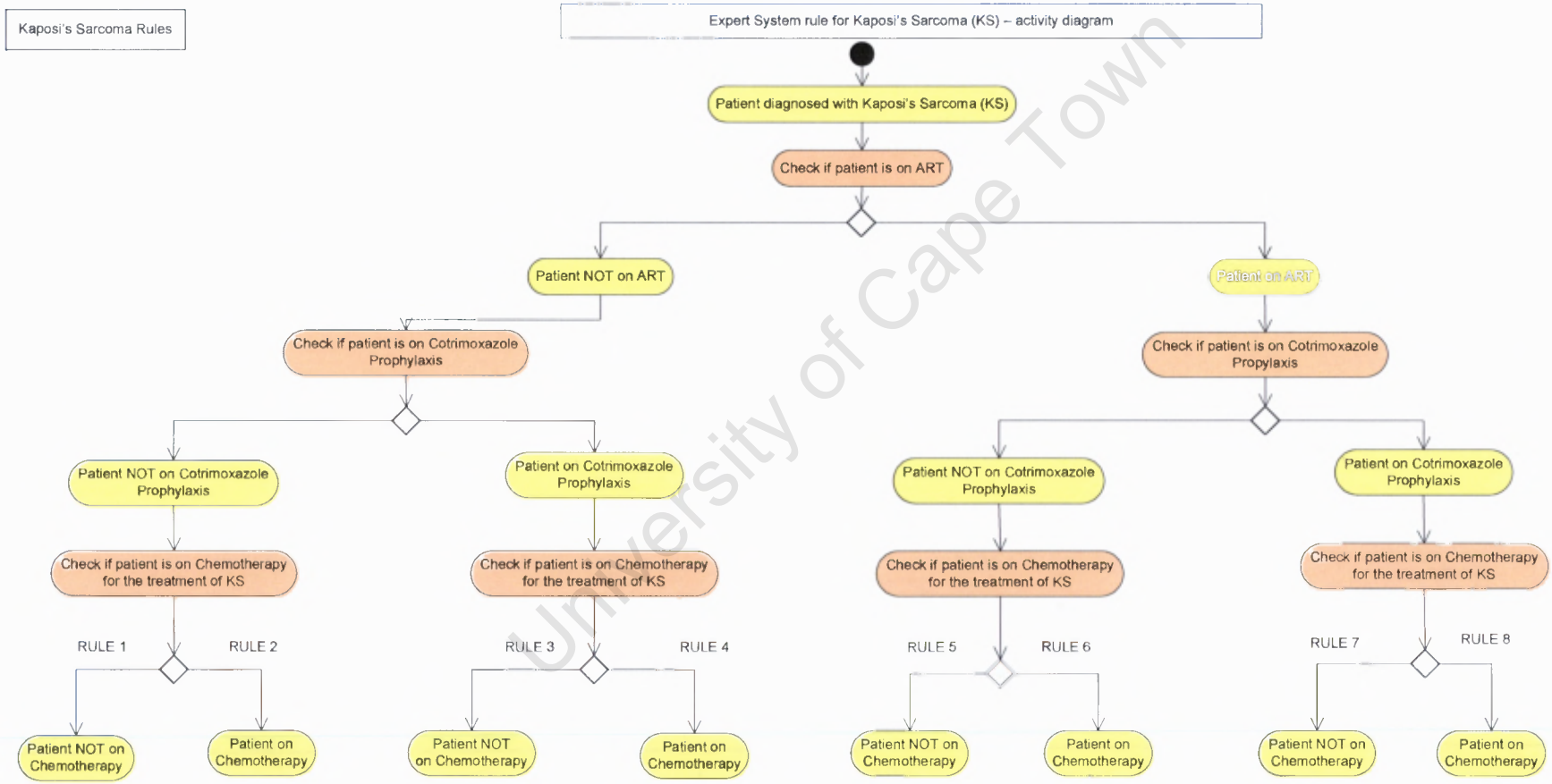


Figure 9: *HIV-expert system* rule diagram for Kaposi's Sarcoma – simplified

4.8.3 Implementation of treatment principles for Cytomegalovirus

Based on the treatment principles, the author defined the rule criteria and rule actions to be applied by the *HIV-expert system*. These are very similar to implementation for Kaposi's Sarcoma with the exception being that the patient needs to be on antiviral therapy for the treatment of CMV. Table 4 summarises the rule criteria and rule action for the Cytomegalovirus rule. Figure 10 is an illustration of the rules (simplified rules for Cytomegalovirus).

Rule Criteria		Rule action	
Description	**Reason**	**Description**	**Reason**
Patient needs to have a hospital diagnosis = Cytomegalovirus	"Entry" criteria for rule check		
Patient needs to be on medication = ART	Treatment principle a)	Level 1 intervention	Detailed discussion with Dr is needed
Patient needs to be on medication = Co-trimoxazole prophylaxis	Treatment principle b)	Level 2 intervention	Less detailed discussion with Dr is needed
Patient needs to be medication = antiviral for the treatment of Cytomegalovirus	Treatment principle c)	Level 1 intervention	Detailed discussion with Dr is needed

Table 4: Summary of rule criteria and rule actions for Cytomegalovirus

4.8.4 Rule diagram for Cytomegalovirus – simplified

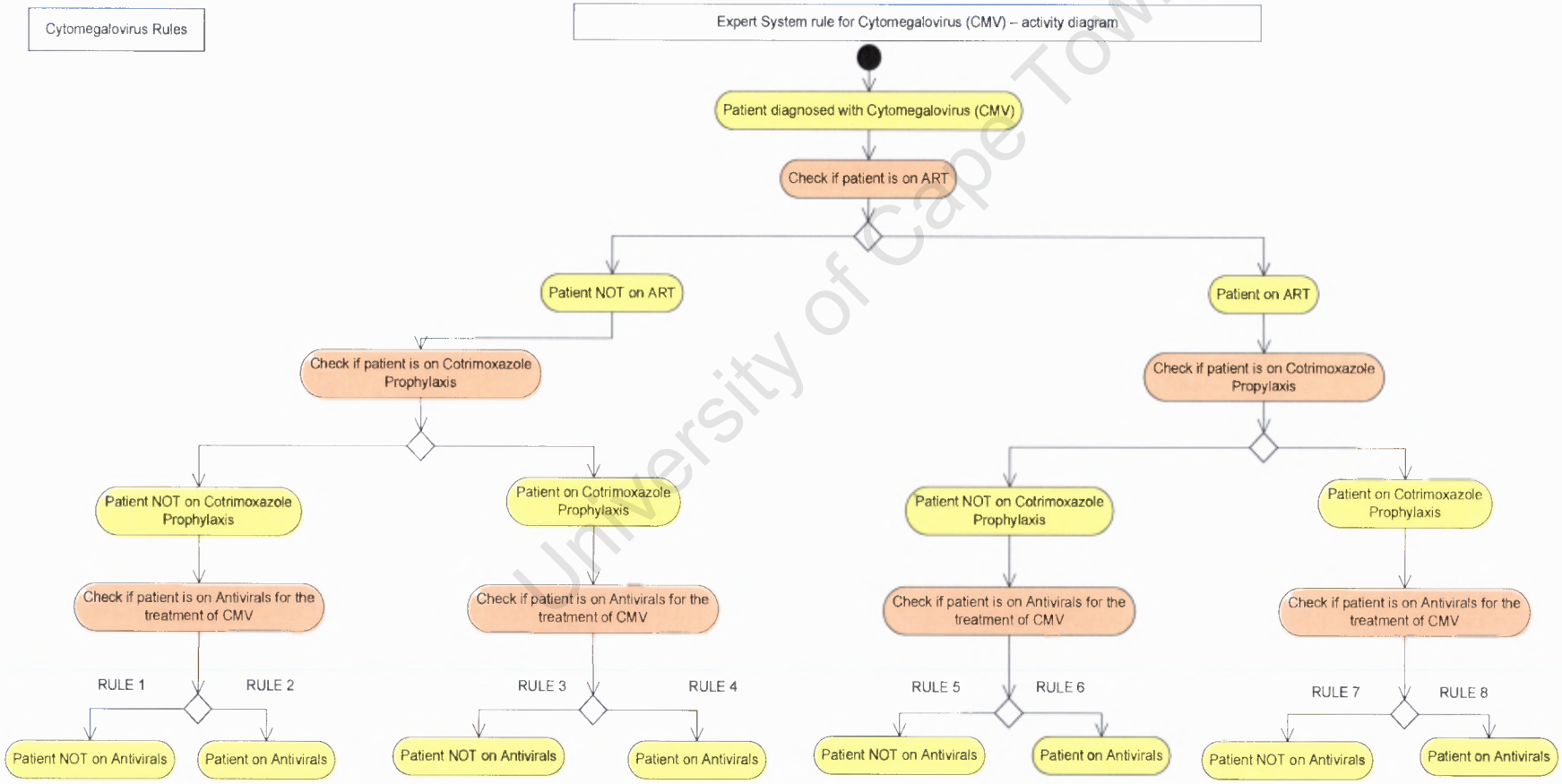


Figure 10: *HIV-expert system* rule diagram for Cytomegalovirus - simplified

Chapter 5: Implementation of the *HIV-expert system*

5.1 Introduction

This chapter gives an overview of how the *HIV-expert system* for the adjudication of hospital data in HIV disease management was implemented. It includes an explanation of rule processing in SQL, importing of diagnosis and medication information for the *HIV-expert system*, SQL database details, rule details, SQL details for the key stored procedures and prototype website details.

In this thesis the author played a dual role as the initial knowledge expert (being a qualified pharmacist) and as the system developer. When selecting rules to test the system, the author consulted various clinical sources. Firstly, to see which hospital diagnosis admissions are being reported in the scientific literature with a focus on the South African situation [Groenewald et al. 2005a] and [Groenewald et al. 2005b]. Secondly, to see which hospital diagnoses would make for interesting database rules (i.e. check multiple complex criteria). Based on this data, two sets of rules for opportunistic infections, Kaposi's Sarcoma and Cytomegalovirus, were selected.

5.2 Overview of rule processing in SQL

The *key* relation for rule processing is the PatientDiagnosis relation, which is updated during the 5 main processing steps as shown below.

```
select PatientID, DiagnosisID, Hospitalname, DoctorName, validFrom, ProcessedDate, InterventionDate
from patientdiagnosis
```

100 %

Results | Messages

	PatientID	DiagnosisID	Hospitalname	DoctorName	validFrom	ProcessedDate	InterventionDate
1	1000	100	ABC hospital	Dr A	2011-12-09 07:37:41.287	2011-12-09 07:38:16.007	NULL
2	1001	101	DEF hospital	Dr B	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
3	1002	100	GHI hospital	Dr C	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
4	1003	100	JKL hospital	Dr D	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
5	1004	100	MNO hospital	Dr E	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
6	1005	100	PQR hospital	Dr F	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
7	1006	100	STU hospital	Dr G	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
8	1007	100	VWX hospital	Dr H	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
9	1008	100	YZA hospital	Dr I	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
10	1009	101	BCD hospital	Dr J	2011-12-09 07:37:41.290	2011-12-09 07:38:16.007	NULL
11	1010	100	EFG hospital	Dr K	2011-12-09 07:37:41.293	2011-12-09 07:38:16.007	NULL

1. Patient Diagnosis hospital data is received:
   A stored procedure ReceiveDiagnosisData is executed and a record is inserted into PatientDiagnosis relation with ValidFrom=GetDate()

2. Patient Meds data is received:
   A stored procedure ReceiveMedsData is executed.

3. Rule processing by the *HIV-expert system*:
   Stored procedures CheckRuleCriteria and ProcessRules are executed. Once processing is complete the PatientDiagnosis relation is updated with the ProcessedDate=GetDate()

4. Recommendation from the rules in the *HIV-expert system*
   This can be viewed on the prototype website. The interventionist (pharmacist) then executes the actions shown on the website. This information is the plan for intervention used when contacting the doctor

5. Intervention complete
   Once the intervention is complete, the user clicks the "complete" button on the prototype website. The PatientDiagnosis relation is updated with InterventionDate=GetDate()

Figure 11 illustrates the rule processing in the *HIV-expert system*.

5.3 SQL Database details

The *HIV-expert system* database and data dictionary are given in appendices 1and 2 respectively.

5.3.1 Relation details

The relations are divided into different types: Main relations (possible inputs (patients, diagnoses, medications) and outputs (EPC, priority, stage, notes), Patient related (link Patient relation and a Main relation), Rules, Rules related (linked to Rules relation) and Processing related (for *HIV-expert System* inference)

Relation number	Relation name	Type of relation	Brief description
1	Patient	Main	Patient demographic data
2	Diagnosis	Main	Hospital diagnosis data
3	Meds	Main	Medicine maintenance data
4	EPC	Main	EPC codes
5	Priority	Main	Priorities e.g. Urgent
6	Stage	Main	1= pharmacist or 2= assistant
7	Notes	Main	Explanations to discuss with doctor
8	MedsDetails	Main	Medicine descriptions
9	PatientDiagnosis	Patient related	Patient diagnoses & process dates
10	PatientMeds	Patient related	Patients and their medications
11	PatientEPC	Patient related	Patients and their one EPC code
12	PatientPriority	Patient related	Patients and their 1 Priority value
13	PatientStage	Patient related	Patients have 1 associated stage
14	PatientNotes	Patient related	Notes applicable to each patient
15	Rules	Rules	Rule details e.g. no. criteria each
16	RuleCriteria	Rules related	Rule antecedents
17	RuleActions	Rules related	Rule consequences
18	MatchOnDiagnosis	Processing related	Patient-rule matches on diagnosis
19	MatchOnMeds	Processing related	Patient-rule matches on meds
20	MatchOnDiagnosisAndMeds	Processing related	Final patient-rule matches
21	PatientAction	Processing related	Patient actions (consequences)

Table 5: List of relations created in the *HIV-expert system* database

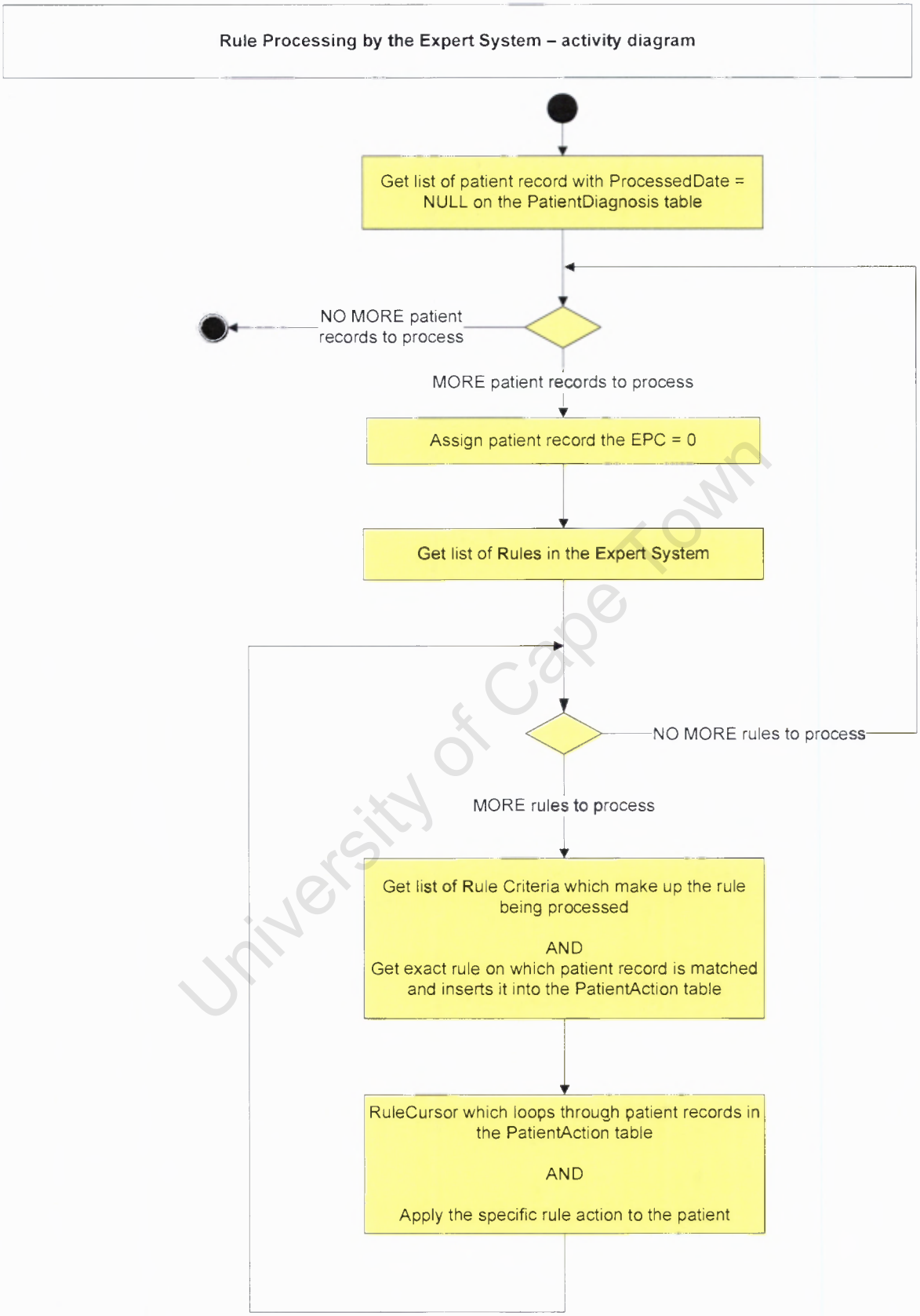


Figure 11: Diagram from rule processing in SQL

5.3.2 Stored Procedure details

The Stored Procedures are listed below:

Stored Procedure number	Stored Procedure name	Type of SQL statement	Relation/s it affects updates	When the stored procedure is executed
1	a_Patient	Insert	Patient	When new *patient* data is received
2	a_Diagnosis	Insert	Diagnosis	When new *diagnosis* data is received
3	a_Meds	Insert	Meds	When new *meds* data is received
4	a_Notes	Insert	Notes	When new *notes* data is received
5	a_Priority	Insert	Priority	When new *priority* data is received
6	a_Stage	Insert	Stage	When new *stage* data is received
7	a_Rules	Insert	Rules	When new *rules* data is received
8	a_RuleCriteria	Insert		When new *rule criteria* data received
9	a_RuleAction	Insert		When new *rule action* received
10	ReceivePatientDiagnosisData	Insert	PatientDiagnosis	When new *diagnosis* data is received
11	ReceivePatientMedsData	Insert	PatientMeds	When new *meds* data is received
12	CheckRuleCriteria	Insert and Update	PatientEPC PatientStage MatchOnDiagnosis MatchOnMeds MatchOnMedsAndDiagnosis PatientAction	When processing new *diagnosis and meds* data
13	ProcessRule ApplyRuleActions NoRuleDiagnosis NoRuleMeds	Insert and Update	PatientNotes PatientEPC PatientPriority PatientStage PatientDiagnosis	When processing new *diagnosis and meds* data

Table 6: List of stored procedures that are executed in the *HIV-expert system* database

5.3.3 Relational schema

Using the convention that the primary key is underlined the relational scheme for the *HIV-expert system* is:

Patient	(PatientID, Title, FirstName, Surname, IDNumber, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
Diagnosis	(DiagnosisID, DiagnosisName, ClinicalCode, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientDiagnosis	(PatientDiagnosisID, PatientID, DiagnosisID, HospitalName, DoctorsName, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate, ProcessedDate, InterventionDate)

Meds	(MedsID, MedsType, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
MedsDetails	(MedsDetailsID, MedsID, MedsType, MedsGroup, MedsGenericName, MedsAbbreviation, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientMeds	(PatientMedsID, PatientID, MedsID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
EPC	(EPCID, EPCDescription, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientEPC	(PatientEPCID, PatientID, EPCID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
Notes	(NoteID, NotesText, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientNotes	(PatientNotesID, PatientID, NoteID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
Stage	(StageID, StageDescription, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientStage	(PatientStageID, PatientID, StageID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
Priority	(PriorityID, PriorityDescription, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
PatientPriority	(PatientPriorityID, PatientID, PriorityID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
Rules	(RuleID, RuleName, NumberOfDiagnosis, NumberOfMeds, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
RuleCriteria	(RuleCriteriaID, RuleID, DiagnosisID, MedsID, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
RuleActions	(RuleActionID, RuleID, Action, NoteID, EPCID, StageID, PriorityID, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
MatchOnDiagnosis	(PatientID, RuleID, DiagnosisID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
MatchOnMeds	(PatientID, RuleID, MedsID, ValidFrom, ValidTo, CreatedUser, CreatedDate, ModifiedUser, ModifiedDate)
MatchOnDiagnosisAndMeds	(PatientID, RuleID)
PatientAction	(PatientID, RuleID, RuleActionID, Action, ActionPriority)

5.3.4 Main relations

The Patient relation contains patient demographic information. This includes: title, name and ID number.

The Diagnosis relation contains the hospital diagnosis information which is important for HIV disease management. The hospital diagnoses that have rules created in the prototype *HIV-expert system* are: (1) Kaposi's Sarcoma (KS) and (2) Cytomegalovirus (CMV). Other diagnosis that are listed in the Diagnosis relation but do not have rules created are: (3) Other Diagnosis and (4) Insulin-Dependent

Diabetes Mellitus. The ClinicalCode attribute refers to the ICD10 international coding standard for diagnoses [World Health Organization 2010].

In the Meds relation, medication information specifically related to the treatment of HIV and related Opportunistic Infections are listed. The MedsType attribute includes ART (Antiretrovirals), Prophylaxis, Chemotherapy, Antifungals and Antivirals. This is an international coding standard for medication [Gibbon et al. 2000]. The MedsDetails relation contains more detailed medication information. MedsGroup attribute refers to the specific medication group in the specific MedsType. For example, for MedsType = ART, there are MedsGroup = Nucleoside Reverse Transcriptase Inhibitors (NRTI), Non-Nucleotide reverse transcriptase inhibitors (NNRTI), Protease Inhibitors (PI) and various combinations of MedsGroup. MedsGenericName attribute refers to the chemical name for medication. For example, for MedsGroup = Nucleoside Reverse Transcriptase Inhibitors (NRTI), there are MedsGenericName = Abacavir, Didanosine, Lamivudine, Stavudine and Zidouvudine. MedsAbbreviation attribute refers to the standard abbreviation for a specific MedsGenericName. For example, for MedsGenericName = Abacavir, the MedsAbbreviation = ABC.

The EPC relation contains the EPC (Electronic Processing Code) information. This is used in the current EPS system and because the new *HIV-Expert system* will be integrated into the current system, it made sense to use the same coding system [Foster 2010]. In the Notes relation, the notes which the pharmacist will read when planning the intervention with the doctor are listed. Specific notes are inserted when specific rules are matched. The Stage relation contains stage information so that the appropriate intervention can be done by staff with the necessary skill level. For example, Intervention level 1 is worked on by pharmacists and Intervention level 2 is worked on by pharmacist assistants. In the priority relation, the priority information is listed. A patient with an urgent priority will therefore be reviewed sooner than the patient with a normal priority.

5.3.5 Patient relations

The patient related relations linked the main tables to the patient tables (see Figure 12). On all the Patient-related relations, a history of all records is kept the current record has a ValidTo attribute of null while previous records have a ValidTo date populated.

PatientDiagnosis links hospital diagnosis information to a patient: 1 patient can be linked to 0 or many diagnosis records. The HospitalName and DoctorName attributes are included so that when the pharmacist does the intervention with the doctor, these details show if the doctor treating the HIV disease (HIV doctor) and the doctor admitting the patient for the hospital diagnosis (hospital doctor) is the same person or from the same practice. These details are especially important if they are not the

same, as the HIV doctor maybe unaware of the hospital admission. ValidFrom and ValidTo indicate the time in which a specific diagnosis record is linked to patient. The ProcessedDate attribute refers to the date the record was processed by the *HIV-expert system*. This is included so that new records to be processed can be identified. The InterventionDate attribute refers to the date the interventionist (pharmacist) contacted the doctor to discuss the action plan.

The PatientMeds relation links the medication information to a patient where 1 patient can be linked to 0 or many meds records, the PatientEPC relation links EPC information to a patient where 1 patient can only be linked to 1 EPC record, the PatientNotes relation links notes to a patient where 1 patient can be linked to at least 1 or many notes, the PatientStage relation links stage information to a patient where 1 patient can only be linked to 1 stage and the PatientPriority relation links priority information to a patient where 1 patient can be linked to 0 or 1 priority records.

5.3.6 Rule and processing relations

The Rule relation contains a list of rules that are coded for rule processing. Each Rule has RuleCriteria and RuleActions (see Figure 13). Once all the RuleCriteria for a specific rule are met, the RuleActions are applied to the specific patient records that meet the RuleCriteria (see Figure 14). The NumberOfDiagnosis attribute refers to the number of diagnosis criteria to be met for this rule to be passed. Similarly the NumberOfMeds attribute refers to the number of meds criteria. The RuleCriteria relation contains rule criteria information where 1 rule record can be linked to 1 or many rule criteria records. DiagnosisID refers to the diagnosis required in the PatientDiagnosis relation for the rule criterion of a specific rule to be met. MedsID refers to the meds needed in the PatientMeds relation for the rule criterion of a specific rule to be met. The RuleActions relation contains rule action information where 1 rule record can be linked to 1 or many rule action records. For example, action = note will have a NoteID in that tuple, referring to the note that will be inserted when the rule action is executed. The EPCID refers to the EPC that will be inserted when the rule action is executed and the StageID to the stage that will be inserted. The PriorityID will be inserted only for the rules that have the action of indicating the patient record as urgent.

The MatchOnDiagnosis relation contains the list of patients that match the criteria for a rule based on diagnosis information where 1 patient and rule combination can have null or many records in this relation. Similarly, the MatchOnMeds relation contains patients that match the criteria for a rule based on medication information. The MatchOnDiagnosisAndMeds relation contains patients that match the rule criteria for a rule based on diagnosis AND medication information.

The final relation is the PatientAction relation that contains the patient record that matches the criteria for a rule and will have the corresponding rule actions executed, where 1 patient and rule combination can have null or many records in this relation.

See Figure 12, 13 and 14 below.

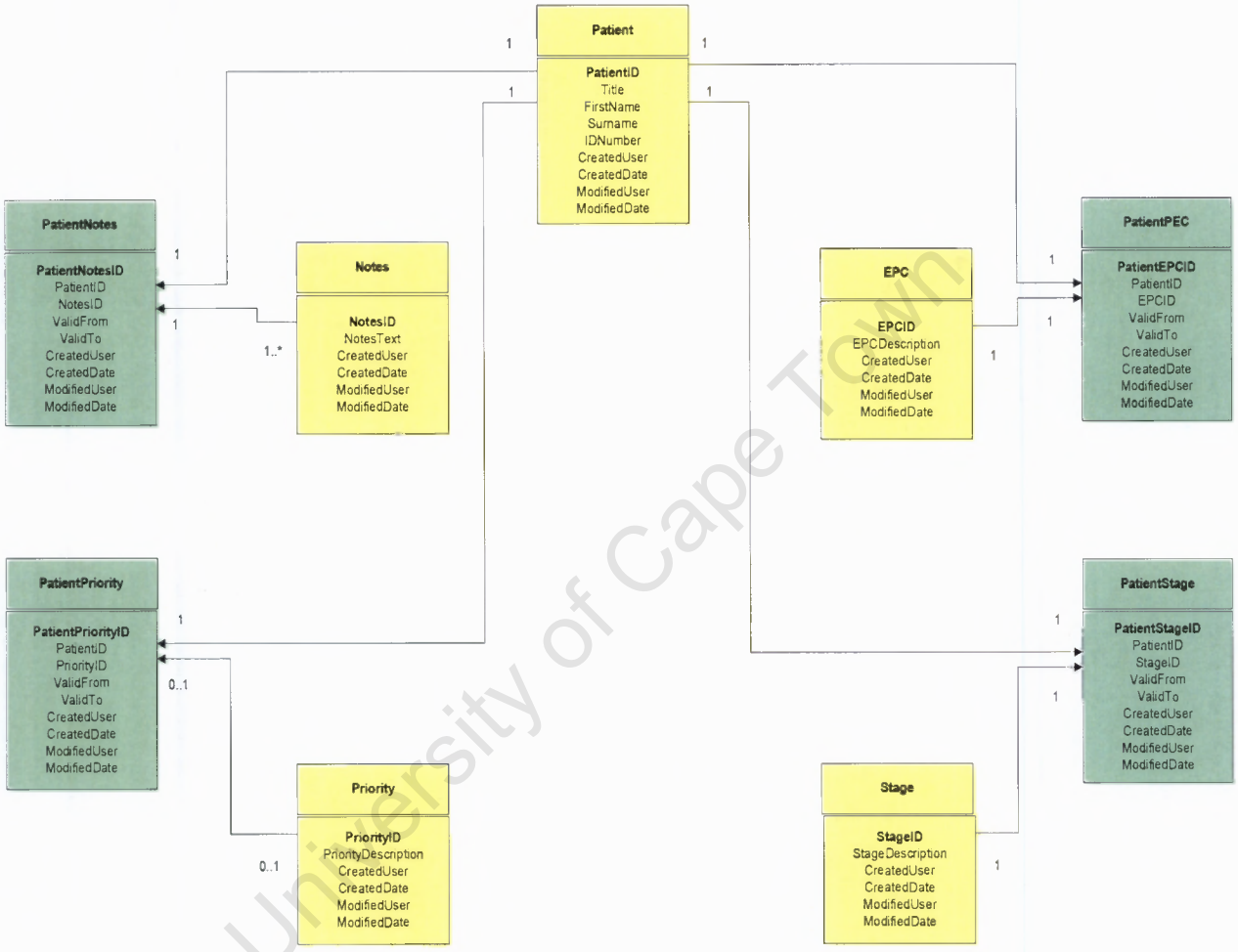


Figure 12: Class diagram – Patient relations in the *HIV-expert system*

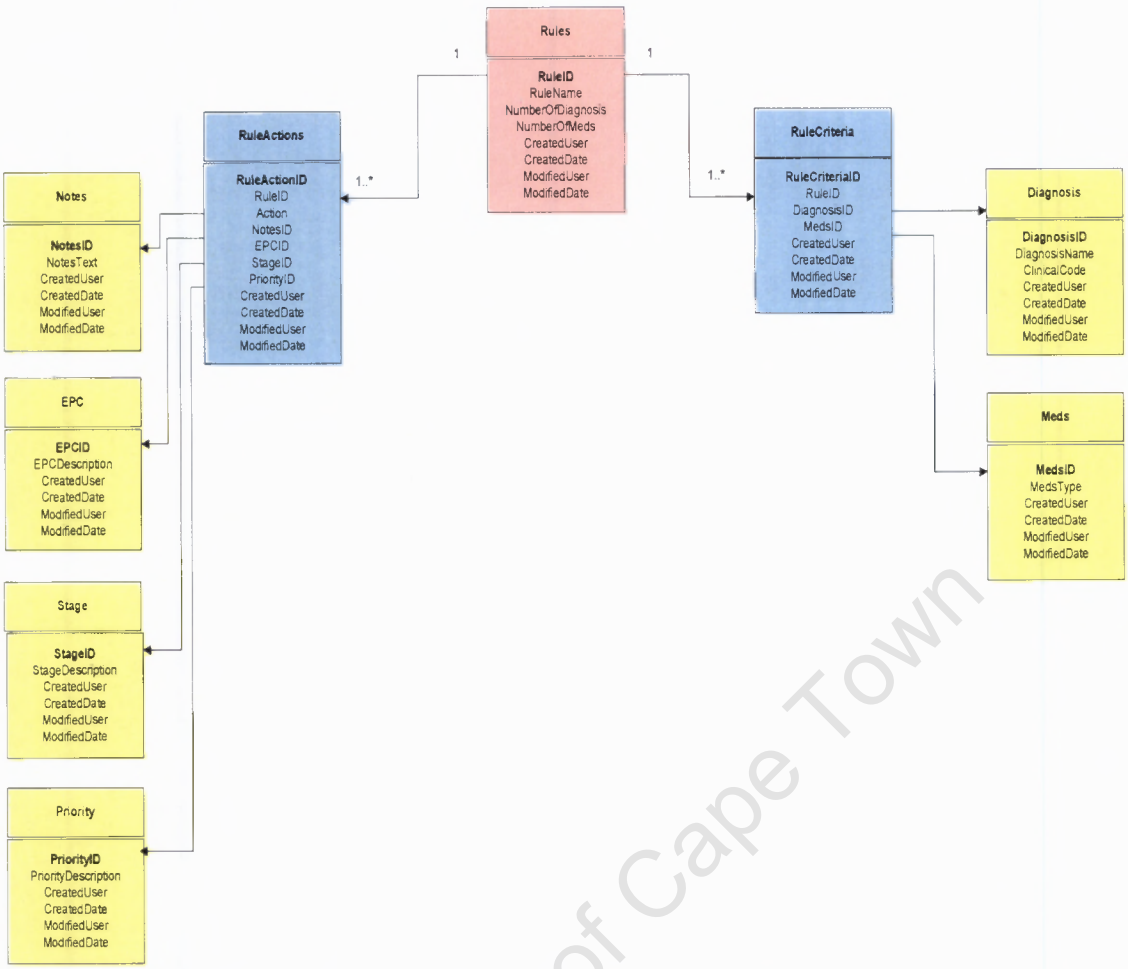


Figure 13: Class diagram 2 – Rules relations in the *HIV-expert system*

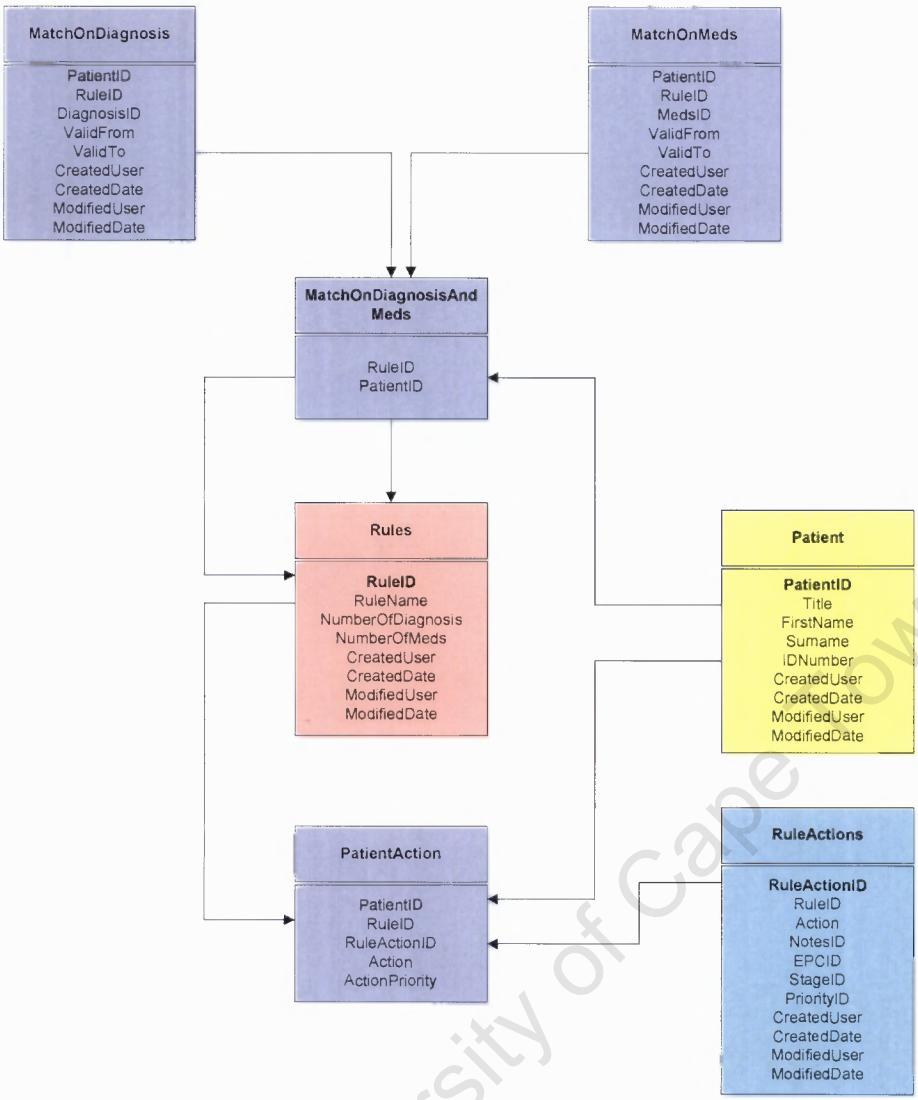


Figure 14: Class diagram 3 – Matched relations in the *HIV expert system*

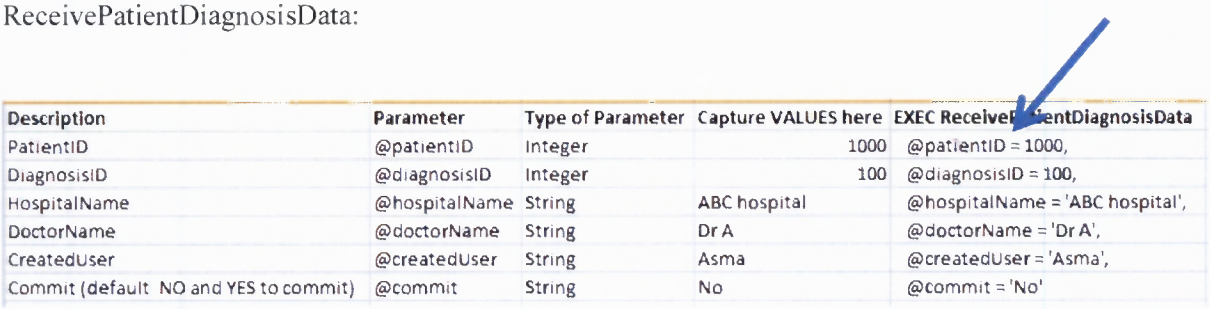
5.4 Importing of diagnosis and medication data

As the user interface is beyond the scope of this work, the diagnosis and medication data was imported from a spreadsheet. The spreadsheet has 2 sheets: user sheet and system sheet. The user sheet is created to capture values for input parameters for the stored procedure. The system sheet uses an Excel formula to populate the input parameters for the stored procedure. For the importing of diagnosis data, the user enters details in the user sheet in Excel, as shown below:

Description	*Capture VALUES here*
PatientID	1000
DiagnosisID	100
HospitalName	ABC hospital
DoctorName	Dr A
CreatedUser	Asma

Figure 15: Screen print of user sheet for Patient ID = 1000

Using the copy and concatenate functions the following is generated for the Stored procedure ReceivePatientDiagnosisData:



Description	Parameter	Type of Parameter	Capture VALUES here	EXEC ReceivePatientDiagnosisData
PatientID	@patientID	Integer	1000	@patientID = 1000,
DiagnosisID	@diagnosisID	Integer	100	@diagnosisID = 100,
HospitalName	@hospitalName	String	ABC hospital	@hospitalName = 'ABC hospital',
DoctorName	@doctorName	String	Dr A	@doctorName = 'Dr A',
CreatedUser	@createdUser	String	Asma	@createdUser = 'Asma',
Commit (default NO and YES to commit)	@commit	String	No	@commit = 'No'

Figure 16: Screen print of corresponding system sheet for PatientID = 1000

It is easy to use the same approach with a "user sheet" in a different format, e.g. as a Comma Separated Values (CSV) file instead. The stored procedure:

```
CREATE PROCEDURE ReceivePatientDiagnosisData
       @patientID int,
       @diagnosisID int,
       @hospitalName varchar (60),
       @doctorName varchar (60),
       @createdUser varchar (60),
       @commit varchar (3)
```

inserts the record into the PatientDiagnosis relation:

```
INSERT INTO PatientDiagnosis(PatientID, DiagnosisID, HospitalName, DoctorName,
       ValidFrom, CreatedUser, CreatedDate)
       VALUES (@patientID, @diagnosisID, @hospitalName, @doctorName,
       GetDate(),@createdUser, GetDate())
```

The importing of meds data is done similarly to importing of the diagnosis data.

5.5 Rule details

The rules created in the *HIV-expert System* are: Kaposi's Sarcoma and Cytomegalovirus. Figures 15 and 16 expand the rule diagrams in section 5.3.4 and 5.4.4 respectively.

5.5.1 Rule diagram for Kaposi's Sarcoma - detailed

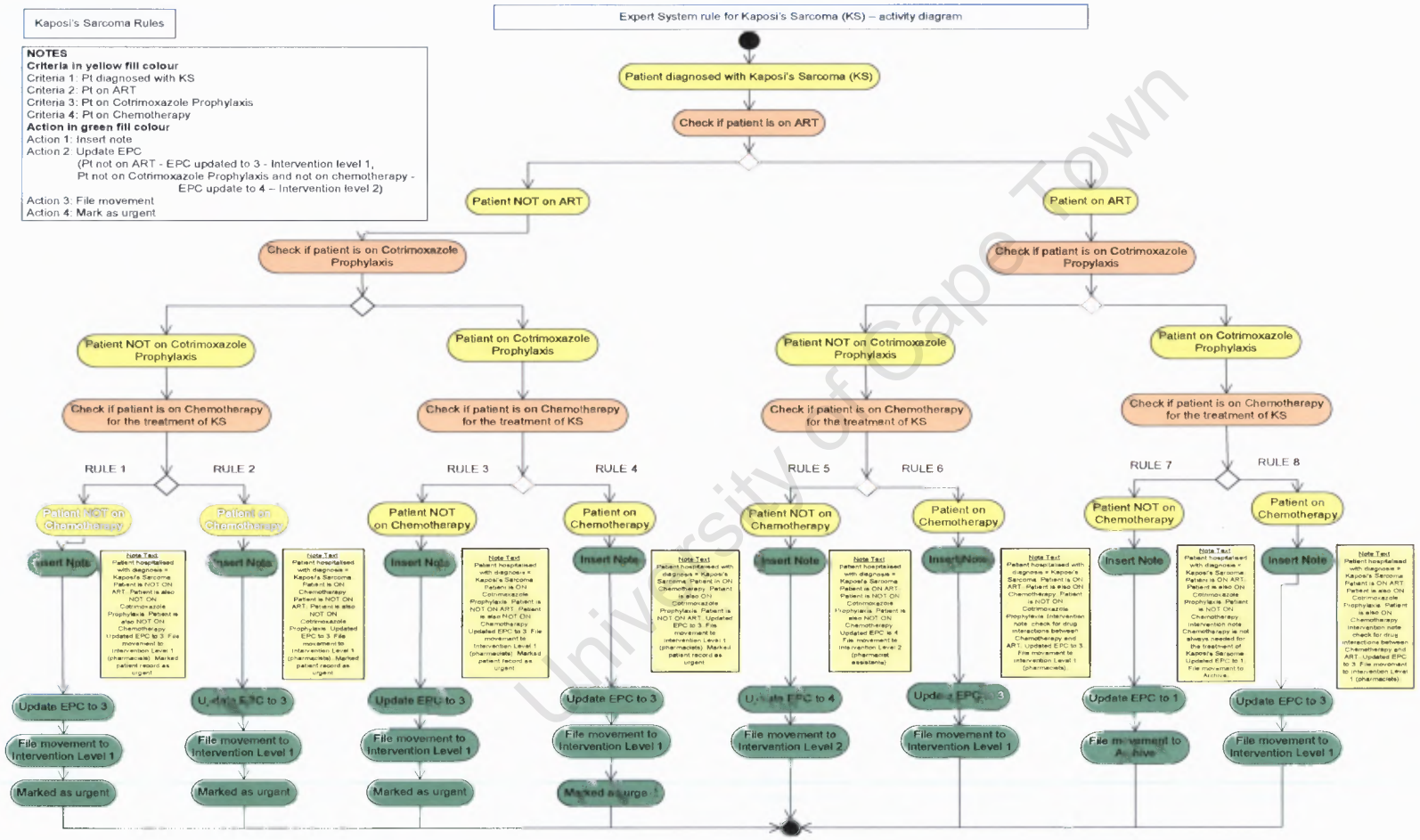


Figure 17: *HIV-expert system* rule diagram for Kaposi's Sarcoma - detailed

5.5.2 Rule diagram for Cytomegalovirus - detailed

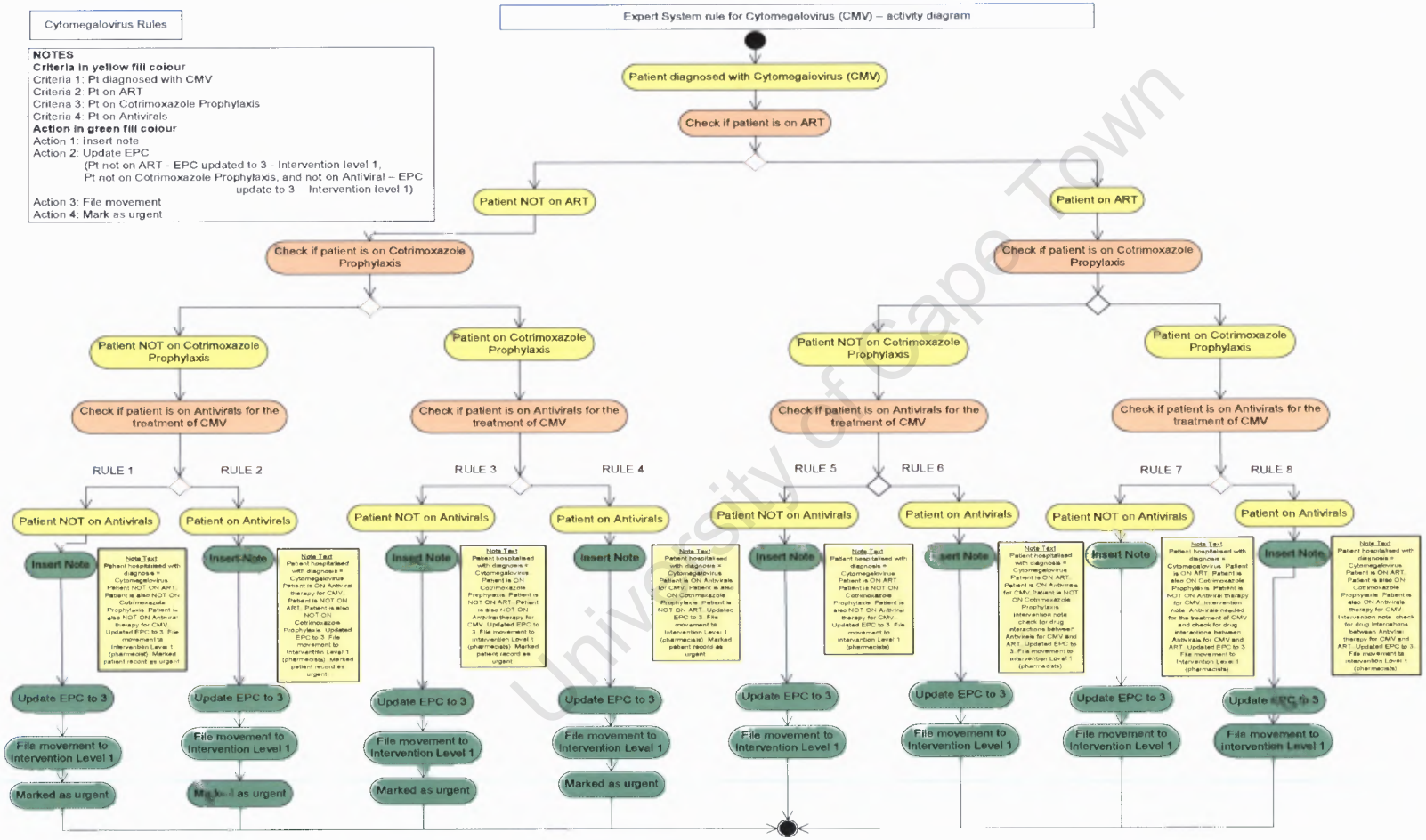


Figure 18: *HIV-expert system* rule diagram for Cytomegalovirus - detailed

5.6 SQL details for stored procedure - CheckRuleCriteria

Below is a diagram that illustrates the steps followed in this stored procedure.

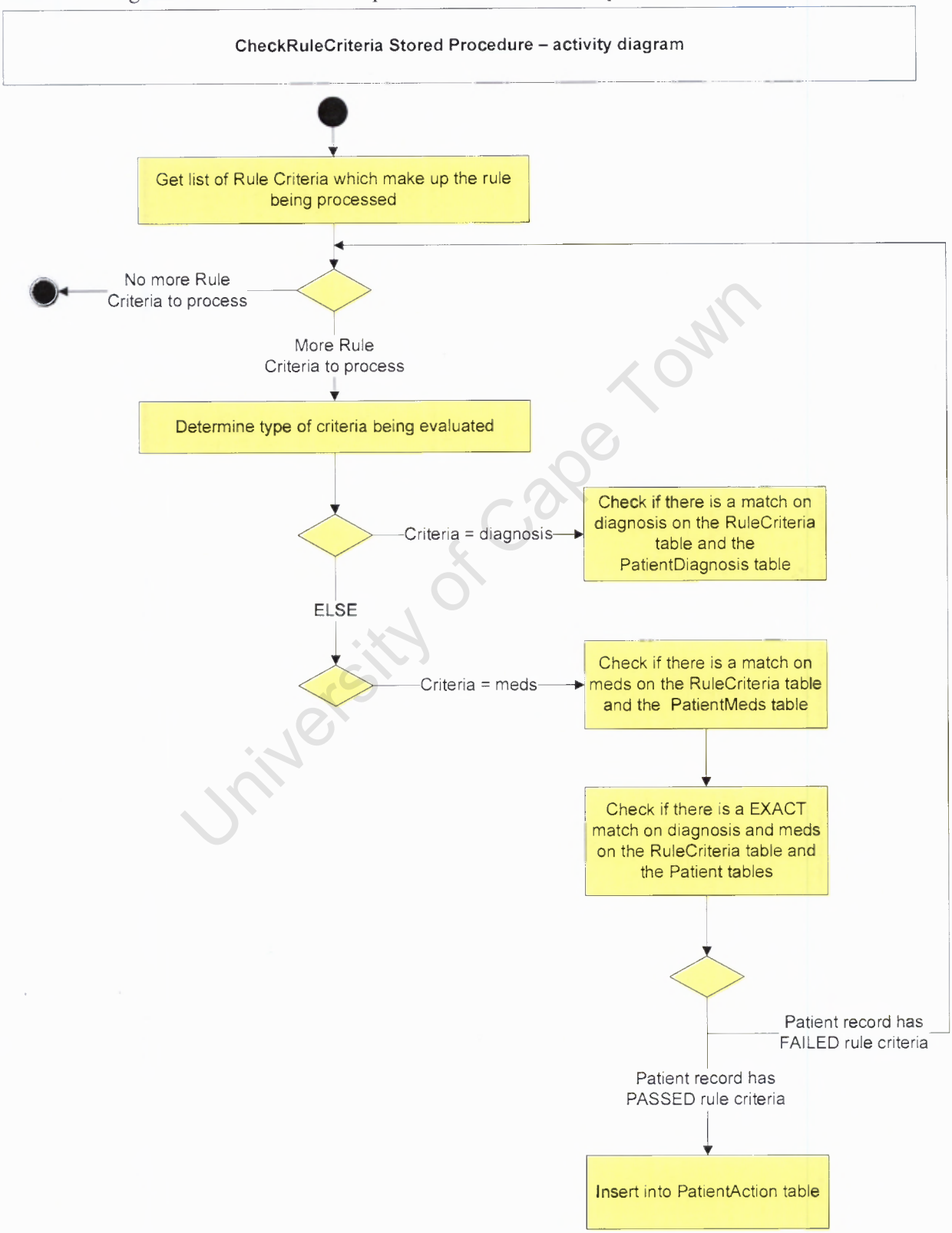


Figure 19: Activity diagram for CheckRuleCriteria stored procedure

First, this procedure finds all the patient records (PatientID) in the PatientDiagnosis relation where the ProcessedDate is null.

- For these records, an insert is done into the PatientEPC relation
- The fields inserted are: PatientID, EPCID, ValidFrom and CreatedUser
- The EPCID is set to 0 which is "unprocessed by electronic screening".
    - The purpose of the EPC ID = 0 is to identify which records need to be processed by the *HIV-expert system*

```
INSERT INTO PatientEPC (PatientID, EPCID, ValidFrom, CreatedUser)
       SELECT PatientID, 0, GetDate(), 'asma'
       FROM PatientDiagnosis
       WHERE ProcessedDate is NULL
```

Next, all the patient records in the PatientEPC relation with EPCID =0 are found

- For these records, an insert is done into the PatientStage relation and
- The fields inserted are: PatientID, StageID, ValidFrom and CreatedUser
- The StageID is set 10 which is "electronic screening"

```
INSERT INTO PatientStage (PatientID, StageID, ValidFrom, CreatedUser)
       SELECT PatientID, 10, GetDate(), 'asma'
       FROM PatientEPC
       WHERE EPCID = 0
```

Next, a check is done to see which records on the PatientMeds relation is matched on the RuleCriteria relation

- For these records, an insert is done into the MatchOnMeds relation
- The fields inserted are: PatientID, RuleID, MedsID, ValidFrom and CreatedUser
- The matching criteria in the where clause is MedsID on the RuleCriteria relation = MedsID on the PatientMeds relation

```
INSERT INTO MatchOnMeds (pm.PatientID, r.RuleID, r.MedsID, ValidFrom,
            CreatedUser)
       SELECT pm.PatientID, r.RuleID, r.MedsID, GetDate(), 'asma'
       FROM PatientMeds pm,
              RuleCriteria r
       WHERE r.MedsID = pm.MedsID
```

Next, a check is done to see which records on the PatientDiagnosis relation is matched on the RuleCriteria relation

- For these records, an insert is done into the MatchOnDiagnosis relation
- The fields inserted are: PatientID, RuleID, DiagnosisID, ValidFrom and CreatedUser

- The matching criteria in the where clause is DiagnosisID on the RuleCriteria relation = MedsID on the PatientDiagnosis relation

```
INSERT INTO MatchOnDiagnosis (pd.PatientID, r.RuleID, r.DiagnosisID, ValidFrom,
            CreatedUser)
       SELECT pd.PatientID,r.RuleID,r.DiagnosisID, GetDate(), 'asma'
       FROM PatientDiagnosis pd,
              RuleCriteria r
       WHERE r.DiagnosisID = pd.DiagnosisID
```

Next, patients that exactly match the criteria of a rule (diagnoses and meds) are found

- For these records, an insert is done into the MatchOnDiagnosisAndMeds relation

```
INSERT INTO MatchOnDiagnosisAndMeds
       (r.RuleID,
        p.PatientID
        )

(SELECT RuleID,PatientID
FROM MatchOnDiagnosis m
GROUP BY RuleID,PatientID
HAVING COUNT (*) = (SELECT NumberOfDiagnosis FROM Rules r WHERE m.RuleID =
                    r.RuleID) -- all for the rule are OK
and COUNT (*) = (SELECT COUNT(*) FROM PatientDiagnosis p WHERE m.PatientID =
                 p.PatientID)) -- exact no. criteria no more

INTERSECT

(SELECT RuleID,PatientID
FROM MatchOnMeds m
GROUP BY RuleID,PatientID
HAVING COUNT (*) = (SELECT NumberOfMeds FROM Rules r WHERE m.RuleID = r.RuleID)
                   -- all for the rule are OK
and COUNT (*) = (SELECT COUNT(*) FROM PatientMeds p WHERE m.PatientID =
                 p.PatientID)) -- exact no. criteria no more
```

Next patient record in the MatchOnDiagnosisAndMeds relation is linked to the RuleActions relation

- For these records, an insert is done into the PatientAction relation

```
INSERT INTO PatientAction
       (m.PatientID,
        m.RuleID,
        ra.RuleActionID,
        ra.Action,
        ra.ActionPriority)
SELECT m.PatientID,
         m.RuleID,
         ra.RuleActionID,
         ra.Action,
         ra.ActionPriority
FROM MatchOnDiagnosisAndMeds m
JOIN RuleActions ra ON m.RuleID = ra.RuleID
```

5.7 SQL details for stored procedure - ProcessRules

This stored procedure runs a cursor named RuleCursor which selects all the patient records in the PatientAction relation and where the Stage in the PatientStage relation is electronic screening.

- For these records, it executes the stored procedure ApplyActions (see 6.11 below)

For each record found in the cursor, the Stored Procedure ApplyActions is executed.

First the cursor selects the PatientID and RuleActionID where the StageID = 10. This is to ensure that only the records that are in the electronic Screening stage will have the cursor applied.

Next, for each record found, the stored procedure named ApplyAction is executed.

```
DECLARE RuleCursor INSENSITIVE CURSOR
FOR
       SELECT pa.patientid, ra.RuleActionID
       FROM RuleActions ra
       JOIN PatientAction pa on pa.ruleID = ra.ruleID
       JOIN PatientStage ps on ps.patientID = pa.patientID
       WHERE ps.StageID = 10 --Stage = Electronic screening
ORDER BY ra.ActionPriority
FOR READ ONLY

OPEN RuleCursor
FETCH NEXT FROM RuleCursor INTO @patientID, @RuleActionID
WHILE (@@FETCH_STATUS <> -1)
BEGIN

       --processing per record is done in SP = ApplyAction
       EXEC ApplyActions
                     @patientID = @patientID,
                     @ruleActionID = @RuleActionID, --from step 1
                     @commit = 'yes'

       FETCH NEXT FROM RuleCursor INTO @patientID, @RuleActionID

END -- of all records in the cursor
CLOSE RuleCursor
DEALLOCATE RuleCursor
END
```

5.8 SQL details for stored procedure - ApplyActions

This stored procedure does a series of steps in sequence. First the rule actions are found:

```
       BEGIN TRAN
       SELECT @action=Action,
                     @note =NoteID,
                     @epcID=EPCID,
                     @stageID=StageID,
```

```
                @priorityID=PriorityID
FROM    RuleActions
WHERE   RuleActionID = @ruleActionID
```

Next, the procedure inserts details into the PatientNotes, PatientEPC, PatientPriority, PatientStage and PatientDiagnosis relations, which together comprise the *HIV-expert system* recommendations. An example is shown below; the other actions are done similarly.

```
IF @action = 'Update stage'
        BEGIN
        UPDATE PatientStage
                SET ValidTo = GetDate(),
                        ModifiedDate = GetDate(),
                        ModifiedUser = 'asma'
                WHERE ValidTo IS NULL --previous stage
                AND PatientID = @PatientID --update for the specific patient
        INSERT into PatientStage (PatientID, StageID, ValidFrom, CreatedUser)
                VALUES (@patientID,@stageID,GetDate(), 'asma')
        END
```

Below is a diagram that illustrates the steps followed in this stored procedure.

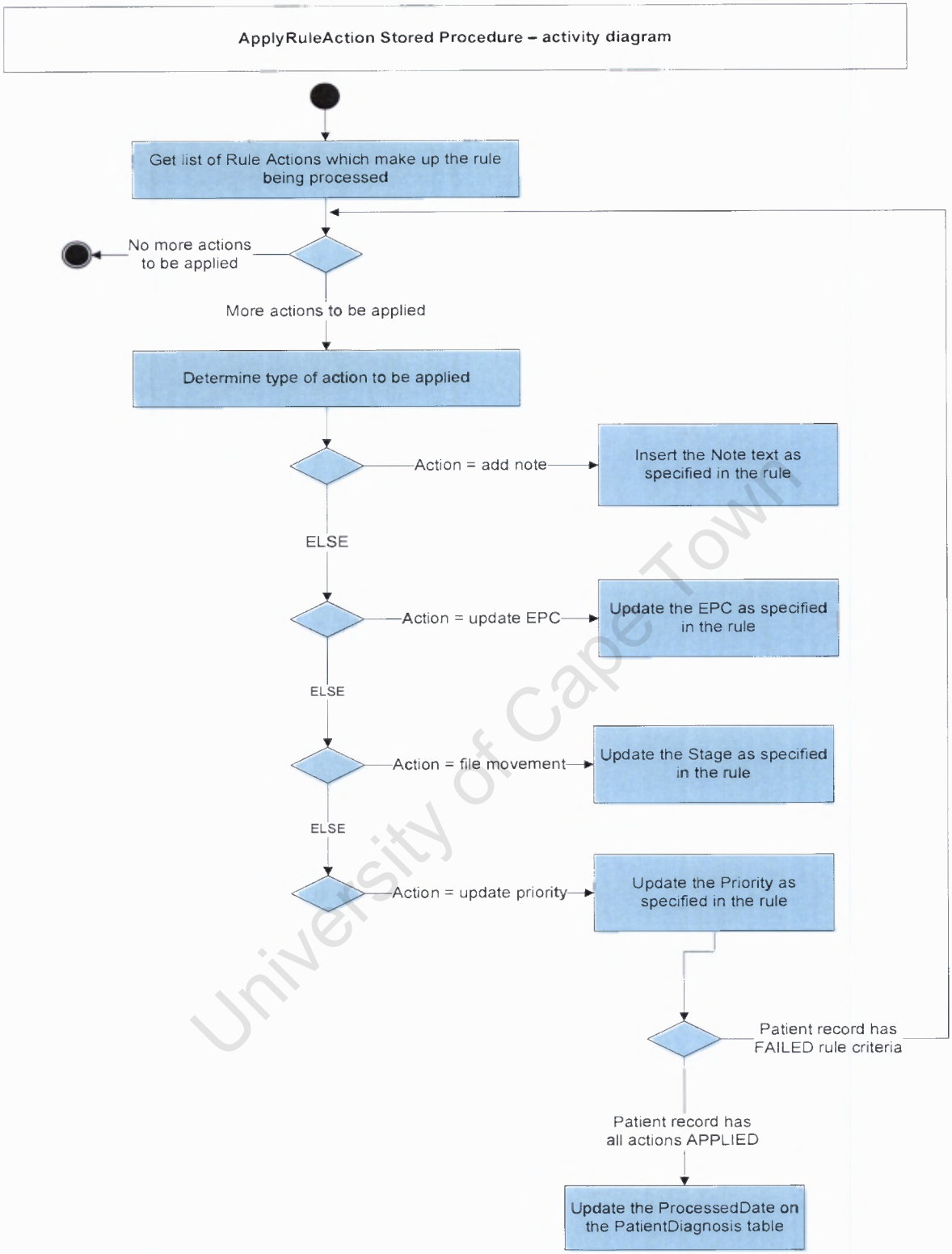


Figure 20: Activity diagram for ApplyRuleAction stored procedure

5.9 SQL details for stored procedure - NoRuleDiagnosis and NoRuleMeds

When processing records, the records which have no diagnosis and no meds are left unprocessed. What this stored procedure does is to mark these records as processed.

5.10 Prototype website

While the user interface is beyond the scope of this work, a prototype website was built for users to view the details in the *HIV-expert system*. The Home and Recommendations pages are illustrated here, with the other screens in Appendix 3.

5.10.1 Home page

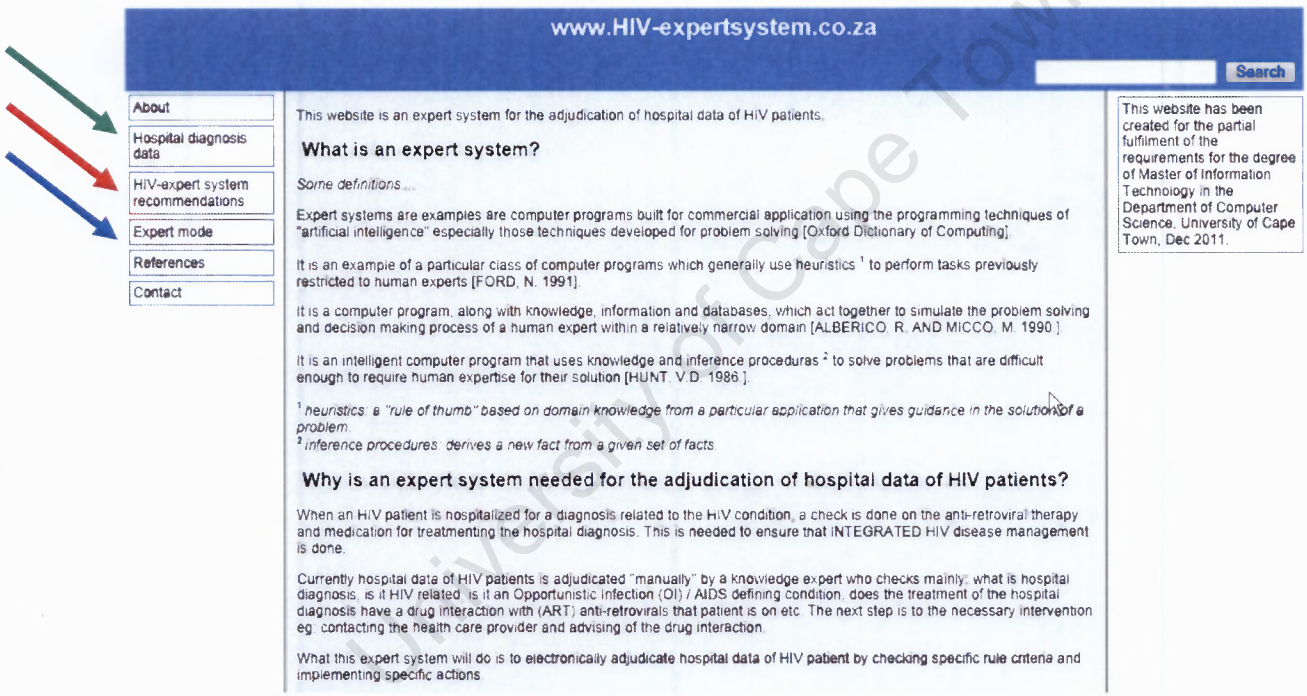


Figure 21: Screen print of the Home Page of website - www.HIV-expertsystem.co.za

On the Home page some context is provided and on the menu on the left hand side, the links to the key screens are displayed. The key screens are: (1) Hospital diagnosis data, (2) *HIV-expert system* recommendations and (3) Expert mode.

The Hospital diagnosis data screen displays the patient, hospital and medication data details. The *HIV-expert system* recommendation system is discussed in more details below. The Expert mode is used by the expert users to check the rule database and to create new rules.

5.10.2 Recommendations from *HIV-expert system*

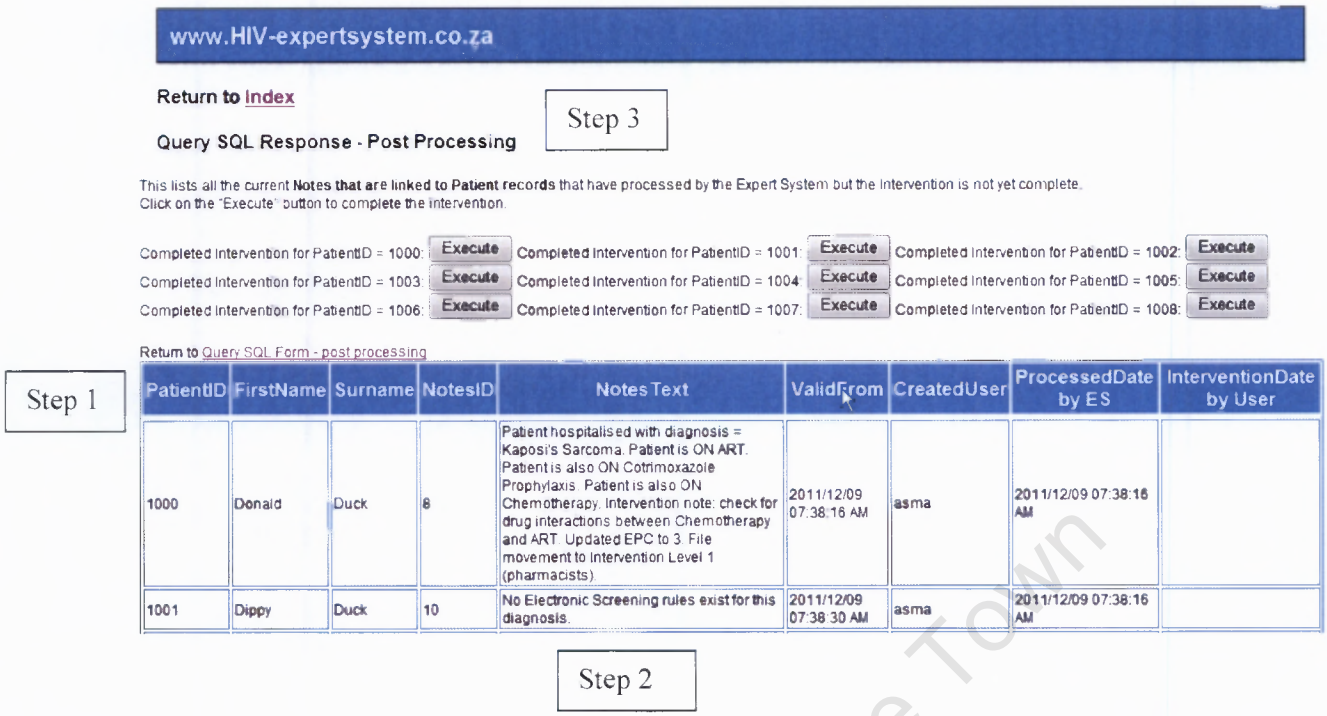


Figure 22: Screen print of the Post Processing Page of the website – www.HIVexpertsystem.co.za

On this page the user will follow 3 steps:

(1) Check patient details

(2) Review the recommendations by the HIV-expert system. This is displayed in the "NotesText" column which is the recommendations for the intervention plan from the HIV-expert system after processing this specific patient record.

(3) Once the actual intervention has been done by contacting the Dr, the user will the click the execute button next to the specific PatientID at the top of the screen. When this button is clicked, the system will then insert an "InterventionDate" into the PatientDiagnosis relations and remove the patient from the display on this page. This is because this page only displays the current cases that need intervention.

5.11 Differences between the current EPS and the *HIV-expert system*

The HIV DMP currently uses a system known as Electronic Process System (EPS). This adjudicates pathology results only. It applies simple IF…THEN logic to test pathology results against pre-defined low and high ranges and categorizes the outcome of the adjudication as routine (no human intervention required) or intervention required. This EPS has been shown to greatly reduce turn-

around time for processing of pathology results and to utilise clinical expert staff time more efficiently as it shows them which cases are non-routine so they can focus on these.

This *HIV-expert system* extends this concept by applying it to hospital data and its associated more complex rules. In this way, an extensible system is created which means a system which can accommodate new rules without any re-programming. This is achieved by designing a database with relations and stored procedures that can encode rule criteria and associated actions and can apply this correctly using only non-procedural code. In this way, new rules can easily be added to database and will be automatically included correctly in subsequent hospital data adjudication, without the need for any re-programming of the system. This is particularly important as the clinical conditions that a patient with HIV can be hospitalized for outnumbers the pathology possibilities, which are limited to around 20 (for example full blood count, liver function test, HIV screening test, HIV resistance test etc.). Clinical conditions which a patient with HIV can be hospitalized for is a continuously growing list. This includes AIDS defining conditions, hospital admission for side effect (adverse drug reactions) to HIV medicines (new products are constantly coming onto the market with its own side effects), as well as hospital admissions related to non-compliance with HIV medicines and resistance to HIV medicines. As more is learnt about HIV, the area of clinical conditions is the one that sees more growth. Hospital data is also more complex to adjudicate because it requires several different criteria that need to be checked and different combinations of criteria lead to different action outcomes.

5.12 Concluding remarks

A relational database and stored procedures were implemented to encode the knowledge and inference engine in an extensible system. The website designed is only a prototype interface where the user can view the recommendations per patient record after it has been processed by the *HIV-expert system*. It was created purely to evaluate accuracy and performance when the system is used by pharmacists.

Chapter 6: Testing and experiment results

6.1 Introduction

This chapter gives an overview of how the experiment was done to evaluate the *HIV-expert system*. It includes a reiteration of evaluation goals. After this, the experiment is outlined and evaluation modes discussed. This is followed by details of the sampling process and details on how the test scenarios were created. Because the survey questions are a core part of the experiment, this is discussed in detail in the next chapter.

6.2 Experiment overview

Experiment design proceeded as follows: identifying the various modes in which to evaluate the *HIV-expert system*, deciding on the survey question format, creating the sampling process, creating the survey questions, scheduling time with the relevant users. Users did not have access to the test scenarios beforehand. During the experiment they were allowed to access any clinical resources (clinical guidelines, website etc.) and in this way, it was like an open book examination for them. User responses per patient record were timed using a stopwatch and users indicated their responses on a spreadsheet, password protected it and saved it.

6.3 Evaluation modes and groups of users

The *HIV-expert system* has been evaluated in 3 different modes: (1) Manual mode, (2) Automated mode and (3) Expert mode. The Expert mode is the evaluation of existing rules and the creation of new rules. The group of users doing this evaluation is group 1 (expert users). The Manual mode is the adjudication of hospital data using only the existing manual process. The Automated mode is the adjudication of hospital data using only the *HIV-expert system*. The group of users who did the adjudication of hospital data in Manual mode and automated mode are the group 2 (end users).

6.4 Overview of how the evaluation goals were tested

6.4.1 Evaluation of rules by a knowledge expert (pharmacist)

In this section, a check was done to ensure alignment of the rules to the treatment principles for specific diagnosis: Kaposi's Sarcoma and Cytomegalovirus. The author has set up the rule in the

system. The checking of rules was done by group 1 (expert users). Feedback is in the form of survey questions.

6.4.2 Evaluation of adjudication by the *HIV-expert system*

In this section, a check was done to ensure that rules were processed correctly per patient record. The author set up the rules in the system. The check of how rules are processed was done by group 1 (expert users). Feedback is in the form of survey. Also in this section is the comparison based on time and accuracy of the same patient record that has been adjudicated in manual mode and automated mode. Adjudication was done by group 2 (end users)

6.4.3 Evaluation of rule creation for a sample new rule

In this section, a new rule was captured on a spreadsheet by group 1 (expert users) and then loaded into the system. A questionnaire was then answered to check the usability of the user interface for setting up new rules. The usability check was done by group 1 (expert users). Feedback is in the form of survey questions. Figure 23 is a diagram which illustrates how the evaluation goals are achieved.

6.5. Sampling process

6.5.1 Groups of users

For the expert mode testing, group 1, 2 clinical experts were selected to take part in this experiment. They were selected based on fact that they currently do the system evaluation of the EPS system (electronic adjudication of pathology results). They are qualified pharmacists and job title is clinical advisor and operations manager respectively. The 2 clinical experts chose to complete the survey questions jointly. For the adjudication testing, group 2, 5 end users were randomly selected qualified pharmacists in the operations and quality assurance department of an HIV DMP. Group 2 (end users) did manual and automated mode adjudication and group 1 (expert users) did rule entry and automated mode adjudication. The manual and automated mode adjudication by end users was needed for the time measurement of the experiment. The automated mode adjudication by the expert users was used in the accuracy measurement.

6.5.2 Patient records

The 2 rules tested in this experiment are: Kaposi's Sarcoma and Cytomegalovirus. The author set the test scenario by making sure that a patient record in the sample matched each rule at least once. A test

scenario was also included where no rule is matched, for example diagnosis of Insulin-Dependent Diabetes Mellitus which is a diagnosis with no expert system rule.

6.5.3 Test scenarios

The test scenarios were supplied on a spreadsheet. It included 20 test scenarios with 10 each covering the diagnosis of Kaposi's Sarcoma and Cytomegalovirus (PatientID's used for Kaposi's Sarcoma was 1000 to 1010 and the PatientID's used for Cytomegalovirus was 1020 to 1030). The user had no forewarning as to what the test scenarios would cover. The element of surprise to a large extent simulates the call centre environment they work in where a doctor could be calling in for advice on anything HIV related. In the list of test scenarios, the author also alternated the diagnoses to ensure that users did not get into a pattern of planning the intervention. Group 2 (end users) evaluated the same test scenarios in manual and automated mode in two separate experiments that ran a few days apart. It was important to run the same test scenarios for the same users so the comparisons can be made.

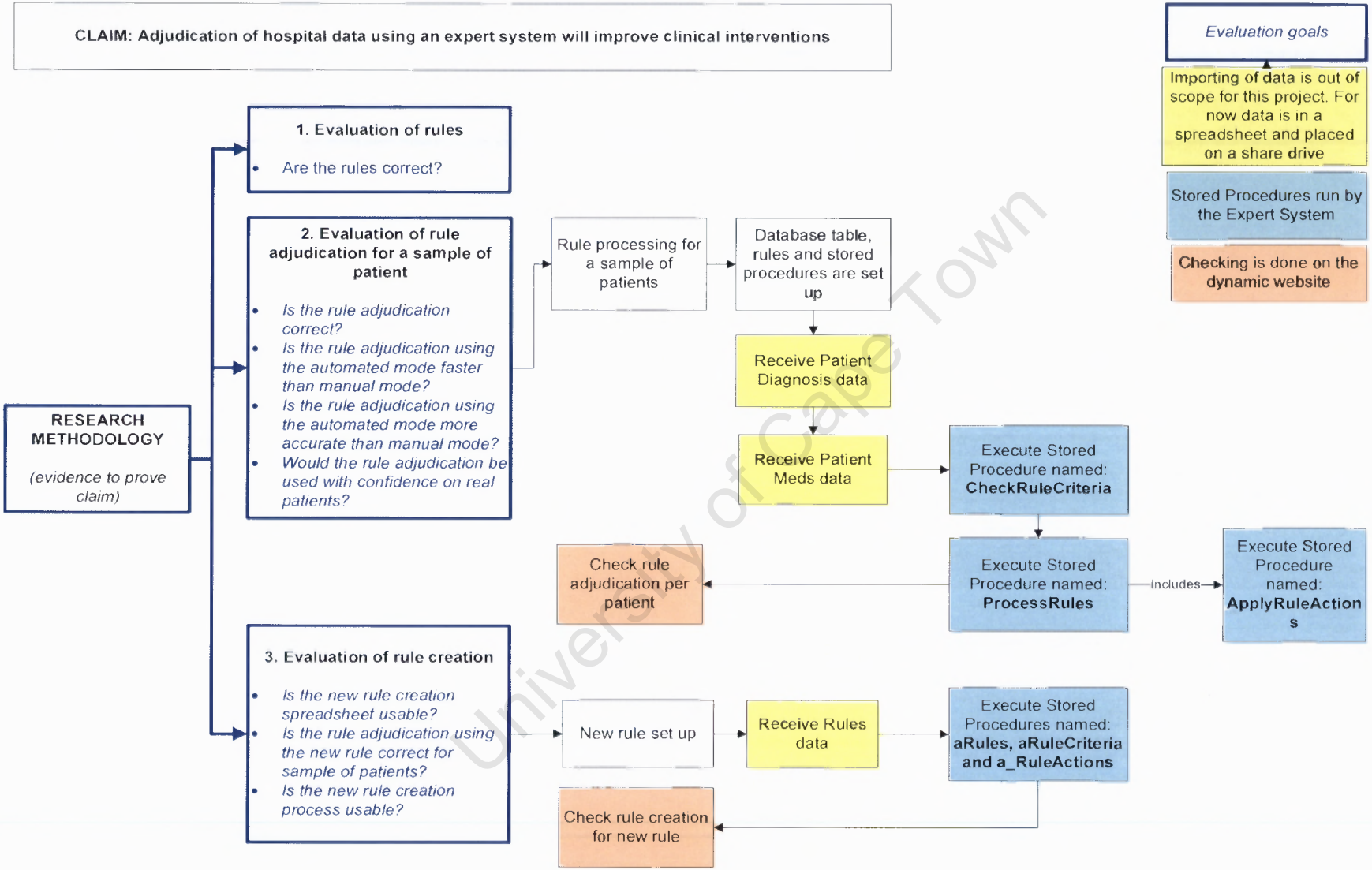


Figure 23: Research methodology and how evaluation goals are achieved

6.6 Experiment details

Table 7 illustrates how evaluation goals are linked to questions. The last column named "evaluation mode" is included to indicate which group of users completed the question in the survey.

Evaluation number	Evaluation goal	Question number	Question detail	Evaluation mode
1	Evaluation of rules	1a and 1b	Is the rule set up correct for existing rules? Prior to implementation, does a clinical expert need to check the rules to be applied by the expert system? Post implementation, does a "human" user need to check each record processed by the rules in the expert system?	Group 1 (expert users)
2	Evaluation of rule adjudication for a sample of patient	2a	Is the rule adjudication in automated mode correct for a sample of patients (20 patients)?	Group 1 (expert users)
		2b	Is the rule adjudication in automated mode faster than manual mode for a sample of patient (20 patients)?	Group 2 and Group 1
		2c	Is the rule adjudication in automated mode more accurate than rule adjudication in manual mode for a sample of patient (20 patients)?	Group 2 and Group 1
		2d	Would the rule adjudication be used with confidence on real patients? Does it improve clinical intervention?	Group 2 and Group 1
3	Evaluation of rule creation	3a	Is the new rule creation spreadsheet usable?	Group 1 (expert users)
		3b	Is the rule adjudication using the new rule correct for a sample of patients (3 patients)?	Group 1 (expert users)
		3c	Is the new rule creation process usable?	Group 1 (expert users)

Table 7: Linking evaluation goals to questions

Experiment method used included doing a pilot experiment before the final experiment. This was needed to address any issues that may arise in final testing. The pilot experiment was done with 1 user and there were no problems found.

6.6.1 Question 1: Evaluation of rules

This question focuses on the evaluation goal 1: Are the existing rules correct? For this part of the experiment, group 1 (expert users) were given the expert system rules for Kaposi's Sarcoma and Cytomegalovirus. The expert users selected to work together in answering the survey questions. The

author acknowledges this may introduce bias but, as experts are by definition rare, it was not possible to find others prepared to do this alone.

6.6.2 Question 2: Evaluation of rules adjudication

This question focuses on the evaluation goal 2:

a. Is the rule adjudication in automated mode correct for a sample of patients (20 patients)?
b. Is the rule adjudication in automated mode faster than manual mode for a sample of patient (20 patients)?
c. Is the rule adjudication in automated mode more accurate than rule adjudication in manual mode for a sample of patient (20 patients)?
d. Would the rule adjudication be used with confidence on real patients? Does it improve clinical intervention?

This question is per patient record and answered for a sample of 20 patient records. The records are divided into 10 records processed by the Kaposi's Sarcoma rules and 10 records processed by the Cytomegalovirus rules.

6.6.2.1 Question 2a: Evaluation of HIV-expert system recommendation

For evaluating this goal, group 1 (expert users) were given the recommendation after the patient record has been adjudicated by the *HIV-expert system.* They were then requested to complete Question 2a on the survey.

6.6.2.2 Question 2b: Test scenario in manual mode (with no HIV-expert system recommendation supplied)

In manual mode, group 2 (end users) were given the test scenario spreadsheet. They were asked to evaluate each of the test scenarios and indicate on the spreadsheet what their intervention plan would be i.e. what checks would they do to prepare for the intervention. The "time taken to prepare the intervention plan" was timed using stop watch. A copy of the user responses on the spreadsheet was kept for the accuracy measurement

6.6.2.3 Question 2b: Test scenario in automated mode (with HIV-expert system recommendation supplied)

In automated mode end users were given the test scenario spreadsheet but this time an additional column was supplied listing the recommendation by the expert system. Five group 2 users completed

the test scenarios in manual mode and automated mode. In every case the second test was completed a few days after the first, with the intention of users not remembering the details of the test scenarios. Responses and time was noted in the same way as above.

6.6.2.4 Question 2c: Test scenario in expert and automated mode (with HIV-expert system recommendation supplied)

For the third part of evaluating this goal, group 1 (expert users) were given the test scenario spreadsheet with recommendation by the expert system supplied. Once again the response and time was noted. Because there is a medical decision being made and the responses are done by trained clinical staff, a high rate of accuracy is expected. Because a high rate of accuracy is expected, the accuracy range of 0-69% is not included. To compare the accuracy of the group 2 (end users) with the group 1 (expert users) the scale selected was:

- 100%
- 90 to 99%
- 80 to 89%
- 70 to 79%

6.6.2.5 Question 2d: Confidence in HIV-expert system

For the fourth part of evaluating this goal, group 2 (end users) completed Question 2d on the survey.

6.6.3 Question 3: Evaluation of rule creation

This question focuses on the evaluation goal 3:

- Is the new rule creation spreadsheet usable?
- Is the rule adjudication using the new rule correct for a sample of patients (3 patients)?
- Is the new rule creation process usable?

The expert users selected to only create one rule branch namely – Cryptococcal meningitis - Rule 1 That means that the question was only answered for this rule. For this part of the experiment, group 1 (expert users) were given the new rule information request spreadsheet to complete. The spreadsheet was then processed to load in the database.

Once it was loaded, the group 1 (expert users) were asked to evaluate if the new rule creation spreadsheet was usable, if the rule adjudication was correct for 3 test patients and if the new rule creation process was usable.

6.7 Test scenario questions

The same list of test scenarios was supplied to group 2 (end users) in both manual and automated mode, with several days between the two tests each time. Three did automated mode first and two did manual mode first. It is important to use the same list of test scenarios so that comparison in time to prepare for intervention could be measured.

6.7.1 Manual mode

This sheet simply listed the patient, diagnosis, ART meds and Chemotherapy/Antiviral if appropriate.

PatientID	Diagnosis	ART	Prophylaxis	Chemotherapy	Antiviral	Prepare intervention plan	Time in min:sec
1000	Kaposi's Sarcoma	AZT, 3TC and EFV	Cotrimoxazole	Bleomycin			
1020	Cytomegalovirus	AZT, 3TC and NVP	Cotrimoxazole		Ganciclovir		
1001	Insulin dependent Diabetes Mellitus	AZT, 3TC and LPV/r					
1002	Kaposi's Sarcoma	TDF, FTC and EFV	Cotrimoxazole				
1022	Cytomegalovirus	AZT, 3TC and LPV/r	Cotrimoxazole				
1003	Kaposi's Sarcoma	TDF, FTC and LPV/r	Cotrimoxazole				
1025	Cytomegalovirus		Cotrimoxazole		Valganciclovir		
1004	Kaposi's Sarcoma	TDF, FTC and NVP					
1024	Cytomegalovirus	TDF, FTC and LPV/r					

Figure 24: User sheet for manual mode users illustrating the various fields

6.7.2 Automated mode

This sheet is the same as what used in the manual mode testing with the only difference being that it has an additional column named "Recommendations from the *HIV-expert system*". These details then assist the user in the preparation of the intervention plan.

PatientID	Diagnosis	ART	Prophylaxis	Chemotherapy	Antiviral	Note from website	Prepare intervention plan	Time in min:sec
1000	Karposi's Sarcoma	AZT, 3TC and EFV	Cotrimoxazole	Bleomycin		Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is also ON Cotrimoxazole Prophylaxis. Patient is also ON Chemotherapy. Intervention note: check for drug interactions between Chemotherapy and ART. Updated EPC to 3. File movement to Intervention		
1020	Cytomegalovirus	AZT, 3TC and NVP	Cotrimoxazole		Gancyclovir	Patient hospitalised with diagnosis = Cytomegalovirus. Patient is ON ART. Patient is also ON Cotrimoxazole Prophylaxis. Patient is also ON Antivirals therapy for CMV. Intervention note: check for drug interactions between Antiviral therapy for CMV and ART. Updated EPC to 3. File movement to		
1001	Broken leg	AZT, 3TC and LPV/r				No Electronic Screening rules exist for this diagnosis.		
1002	Karposi's Sarcoma	TDF, FTC and EFV	Cotrimoxazole			Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is also ON Cotrimoxazole Prophylaxis. Patient is NOT ON Chemotherapy. Intervention note: Chemotherapy is not always needed for the treatment of Kaposi's Sarcoma. Updated EPC to 1. File movement to		

Figure 25: User sheet for automated mode users illustrating the various fields

6.8 Experiment results

The experiment involved 2 clinical expert users and 5 end users who completed the list of test scenarios in manual mode and automated mode. The author is most grateful for them for being available to assist with the experiment.

During the experiment, observation was noted, with user feedback and most importantly a record of the responses kept in Excel. A summary of the responses are listed in tables. The details of responses to survey questions are listed in the Appendix 5.

6.8.1 Question 1: Evaluation of rules

Kaposi's Sarcoma rules and Cytomegalovirus rules were evaluated separately with identical results, which are shown in Table 8.

Question	Statement	Response
Question 1a.1	The rules are perfectly correct i.e. the recommendations are as expected	Strongly disagree
Question 1a.2	The rules have some major errors e.g. rule recommendation incorrect	Strongly agree
Question 1a.3	The rules have some minor errors e.g. text changes to notes	Agree
Question 1a.4	The rules are perfectly complete e.g. no missing criteria	Agree
Question 1a.5	The rules are clear, concise, unambiguous and understandable	Disagree
Question 1a.6	The rules are perfectly consistent and do not conflict with each other	Disagree
Question 1a.7:	Prior to implementation, the rules do not have to be checked by a clinical expert. The rules can be applied as is	Strongly disagree
Question1a.8	Once the rules have been checked by clinical expert, the rules are usable and perfectly safe to apply in practice. Post implementation, a "human" user does not need to check each record processed by the rules in the expert system. I have complete confidence in the application of the rules in practice.	Strongly agree

Table 8: Result details for Question 1a - Rule Evaluation

6.8.2 Question 2: Evaluation of adjudication

Question 2a: Is the rule adjudication in automated mode correct for a sample of patients (20 patients)? Each case was evaluated separately, with identical results as show in Table 9.

Question	Statement	Response
Question 2a.1	The rule adjudication for Patient ID = 1000 perfectly correct i.e. the recommendations are as expected	Strongly agree

Table 9: Result details for Question 2a - Adjudication Accuracy for Patient 1000

Question 2b: Is the rule adjudication in automated mode faster than manual mode for a sample of patient (20 patients)? The time taken to plan for intervention for each test scenario was measured for manual mode and automated mode. The average time taken in each mode was then calculated, and is shown in Table 10. It was found that the adjudication of hospital data in the automated mode is 53% faster than manual mode. The time comparison between manual mode and automated mode was then done: (1) per patient ID (See chart 1) and (2) per diagnosis (See chart 2).

Question	Statement	Time in seconds to plan for intervention in Manual mode	Time in seconds to plan for intervention in Automated mode
Question 2b.1	The rule adjudication time for Patient ID = 1000 to 1010 and 1020 to 1030 per mode was as follows:	1712.00	902.67

Table 10: Result details for Question 2b - Average adjudication times

Question 2c: Is the rule adjudication in automated mode more accurate than rule adjudication in manual mode for a sample of patient (20 patients)?

Question	Statement	Average % Accuracy in Manual mode
Question 2c.1	How accurate was the rule adjudication in manual mode (compare with system rules checked by clinical expert) for sample of 20 patients?	92

Table 11: Result details for Question 2c - Adjudication accuracy

In this section, the author reviewed the accuracy of planned intervention from the manual mode end users and compared then with the planned intervention from the expert users. This was done as follows: the expert user responses were used as the 100% mark, a review was then done of the 5 manual mode user responses and subtracted 10% for any major error and then *average* accuracy was then calculated. It was found that the adjudication of hospital data in the manual mode was 92% compared with 100% accuracy in automated mode.

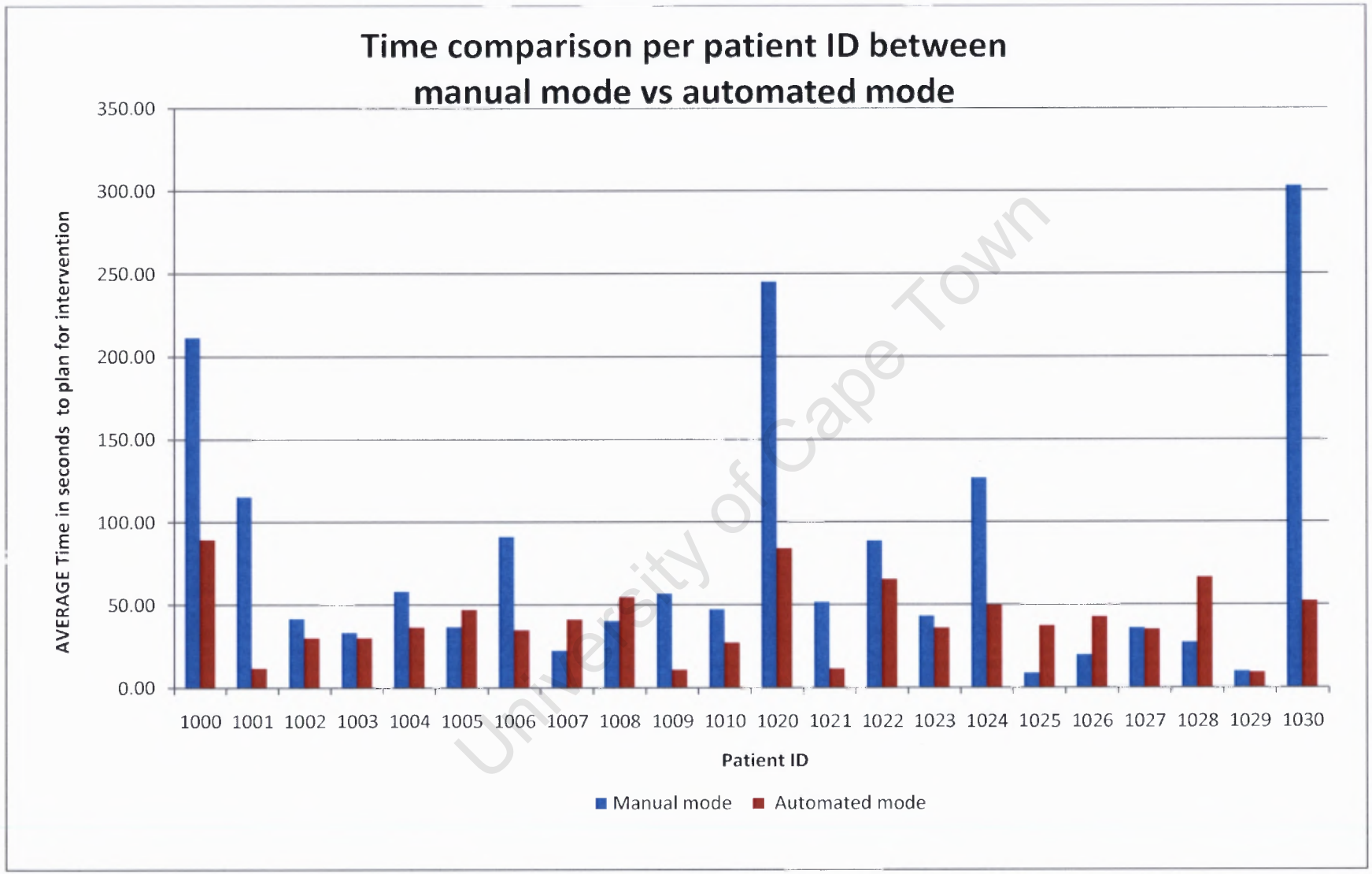


Chart 1: Average Time comparison per patient ID

Note Patient ID's used for Kaposi's Sarcoma were1000 to 1010 and the PatientID's used for Cytomegalovirus were1020 to 1030.

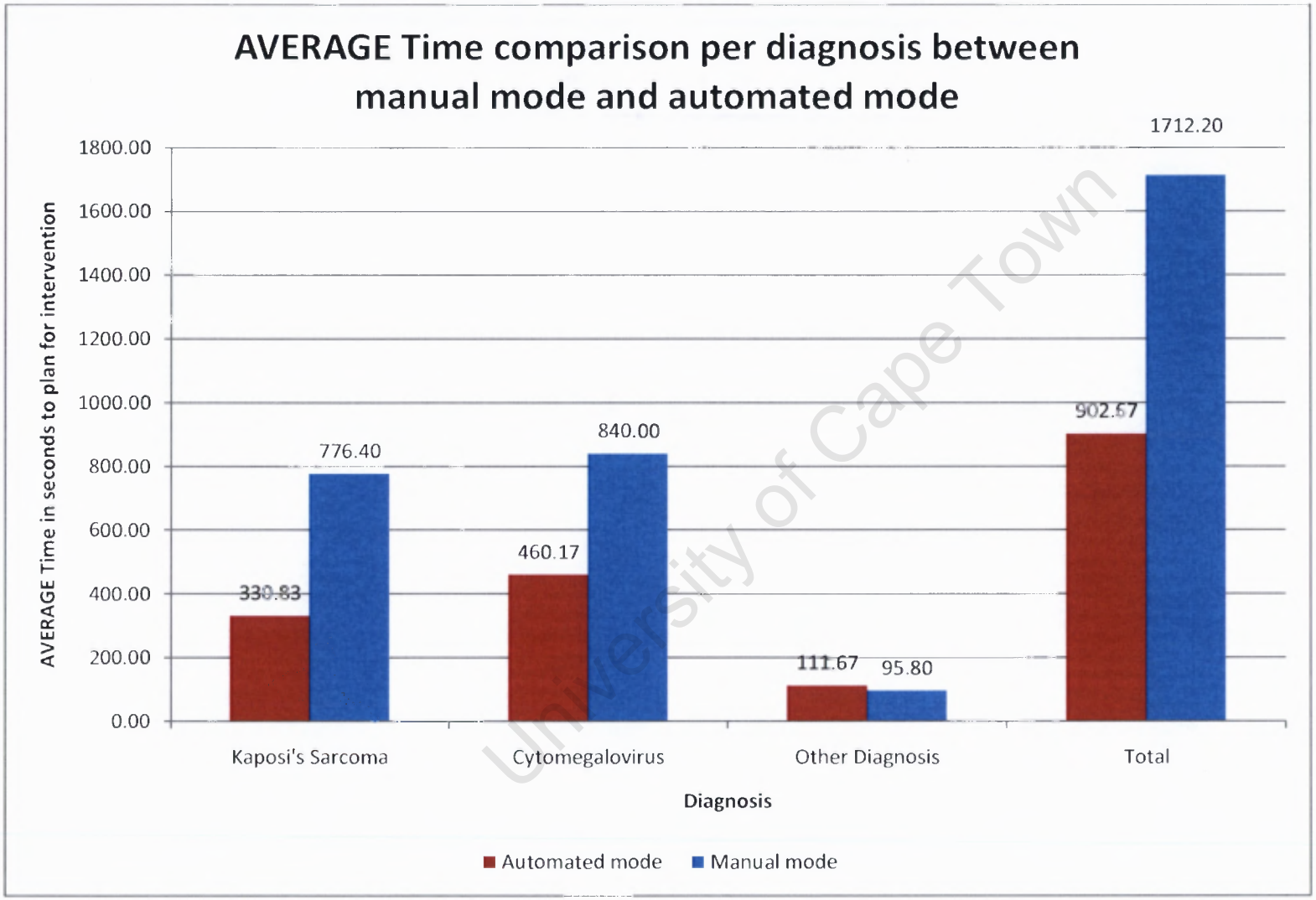


Chart 2: Average Total Time comparison per Diagnosis

Question 2d: Would the rule adjudication be used with confidence on real patients? Does it improve clinical intervention?

Question	Statement	Response	Number of users
Question 2d.1	Does the rules adjudication save time?	Strongly agree	5
Question 2d.2	Is the rules adjudication more accurate	Strongly agree	4
Question 2d.2	Is the rules adjudication more accurate	Agree	1
Question 2d.3	Is the rules adjudication usable and perfectly safe to apply in practice? I have complete confidence in their application	Strongly agree	5
Question 2d.4	If the rules adjudication is NOT usable and NOT perfectly safe to apply in practice. What needs to be changed?	Strongly disagree	4
Question 2d.4	If the rules adjudication is NOT usable and NOT perfectly safe to apply in practice. What needs to be changed?	Disagree	1

Table 12: Result details for Question 2d - user opinion

The 5 user responses are similar with the only difference on question 2d.2 and question 2d.4 between "strong disagree" and "disagree". On the key questions (2d.1 and 2d.3) there was complete agreement from all users.

6.8.3 Question 3: Evaluation of rule creation

Question 3a: Is the new rule creation spreadsheet usable?

Question	Statement	Response
Question 3a.1	New rules information was entered on a spreadsheet. Was the information requested clear, concise, unambiguous and understandable	Strongly agree

Table 13: Result details for Question 3a

Question 3b: Is the rule adjudication using the new rule correct for a sample of patients (3 patients)?

Question	Statement	Response
Question 3b.1	The rule adjudication for Patient ID = 1040 is perfectly correct i.e. the recommendations are as expected	Agree
Question 3b.2	The rule adjudication for Patient ID = 1041 is perfectly correct i.e. the recommendations are as expected	Agree
Question 3b.3	The rule adjudication for Patient ID = 1042 is perfectly correct i.e. the recommendations are as expected	Agree

Question 3b.4	The new rules loaded had some major errors	Strongly disagree
Question 3b.5	The new rules loaded in the database had some minor errors	Agree

Table 14: Result details for Question 3b

Question 3c: Is the new rule creation process usable?

Question	Statement	Response
Question 3c.1	Based on the answers in questions 3a and 3b, the rules adjudication is usable and perfectly safe to apply in practice. I have complete confidence in their application	Agree

Table 15: Result details for Question 3c

6.9 Analysis of experiment results

6.9.1 Question 1: Evaluation of rules

A reminder of the process followed is that as the database designer, the author was also the knowledge engineer (clinical qualification is a pharmacist) in setting up the rules in the database. Only after the HIV expert system had been implemented, was this sent to clinical experts for review. In the discussion with expert users after the response was received, the reasoning behind their responses are as follows:

- The rules were not perfectly correct and had some major error because branch 7 and 8 of the Kaposi's Sarcoma and Cytomegalovirus rules were incorrect.
- The rules also had some minor errors in that the note inserted only specified which treatment the patient was NOT on and did not indicate which treatment the patient was on.
- There was agreement the rules are complete.
- The rules were considered unclear in view of the notes not being specific enough.
- There was strong disagreement that the rules can be applied as is. It was felt that the checking of rules by a clinical expert prior to implementation is critical to the success of rule processing
- There was strong agreement that once the rules have been checked, they are safe to apply.

Based on the clinical expert recommendations, the rules were updated. The updated rules were reviewed by the clinical expert for a second time, after which the clinical experts responded positively to Question 1a.8 and 1b.8. The lesson learnt from these responses is that in retrospect the rules should have been reviewed by a clinical expert before testing.

6.9.2 Question 2: Evaluation of adjudication

6.9.2.1 Question 2a:

There was strong agreement that the rule adjudication was correct for Patient ID = 1000 to 1020. Note, this survey question was answered after their changes to rules in question 1 was done in the database. A positive response to this question validates the fact that rule processing by the *HIV-expert system* is correct.

6.9.2.2 Question 2b:

It was found that the adjudication of hospital data in the automated mode is approximately 50% faster than manual mode (53% faster in this experiment). This has significant impact in a real world HIV disease management program (DMP) operations environment where efficiency is constantly being strived for. Because the plan for intervention time in the automated mode is faster, more patient records can be reviewed and users will be more productive.

6.9.2.3 Question 2c:

It was found that the adjudication of hospital data in the manual mode had a 92% accuracy compared with 100% accuracy in automated mode. In this experiment setting, manual mode users had access to resources but despite this some users still made errors. By using the *HIV-expert system* the error margin will be reduced. Once again in an HIV DMP where quality assurance and accuracy are important factors, this will further validate implementing this system.

6.9.2.4 Question 2d:

Users found the system improved speed and accuracy and were confident that it could be used safely on real patients. In the author's view, this is the most critical question in the survey. It was responded to by expert users and supported by comparison of rule adjudication times and accuracy.

6.9.3 Question 3: Evaluation of rule creation

6.9.3.1 Question 3a:

This was quite positive feedback in that the expert users were not intimidated by the information request on the New Rule spreadsheet. The spreadsheet has adequately hidden the technical details but at the same time achieved correct user input of new rules.

6.9.3.2 Question 3b:

The expert users completed this survey question once they have checked the loading of new rules in the database. The one minor error they found was that the very last word in the note ("urgent") was truncated (to "urgen"). This was easily fixed in the database when it was detected. This was a minor error on the developer side. This was quite positive feedback based on expert user checking of 3 patients in the test sample group.

6.9.3.3 Question 3c:

There was agreement that the new rule set up is usable. From this it is likely that the new rule process can be extended to include updating of existing rules using the same approach. Once this is in place, it will reduce the time the developer needs to code new rules and update existing rules because the spreadsheet can be completed by expert users and the knowledge base automatically updated accordingly.

6.10 Concluding remarks

Setting up the experiment was challenging because, the author was dependant on user availability and time. In setting up the questions and answers selection, it was critical to link it back to the specific evaluation goal and avoid the questionnaire being too long. See Appendix 4 for screen prints of the survey questions. When the author set the test scenarios, pretty standard responses were expected from users but when the author sat down doing the survey by interview, timing their responses, observed how the search for information and based on the additional questions they asked, the author found different users used different resources. The diagnosis selected for this experiment (Kaposi's Sarcoma and Cytomegalovirus) are not common interventions which is dealt with on a daily basis so some of the respondents were not as prepared as they would have been should a more common diagnosis (such as Tuberculosis or Pneumonia) have been selected. In the observation of users completing the test scenarios, the author found that users consult the following 3 resources:

- An Aid for Aids (AfA) hosted intranet site which list the AfA guidelines. These include an alphabetical listing of the disease for information. (www.aidforaids.co.za)
- Hard copies of the clinical guidelines
- International Drug interaction website (www.hiv-druginteractions.org)

Consulting the resources in the manual mode was a large contributing factor in the time calculation. Most users used the first test scenario to fully read up on the section in the guidelines and in this way

the time measured on future interventions was reduced (for example first test for KS was measured at 10 minutes while the average over the rest of the KS cases was 3 minutes). Internet connectivity to the International drug interaction website was also a large contributing factor in the time spent by the one user who used it.

It was of interest to see that the resources were consulted for the test scenarios done in manual mode and hardly ever in the test scenarios done in the automated mode. When questioned about this, the respondents said that "this is not needed because the recommendation from the *HIV-expert system* tells me what I would have looked up in the resources". Future work on the *HIV-expert system* is that the URL for the resources used should be included on the user interface.

Chapter 7: Conclusion

7.1 Summary

A review of the current system that does the adjudication of pathology results and the success of that system in improving efficiency and clinical intervention was a main driving force in developing an expert system for hospital data adjudication in an HIV DMP. In the field of medical informatics, there are various rule-based expert systems in use, and this approach was most suitable for development. In discussions with clinical staff, hospital data came up as one of the top areas the clinical staff felt would benefit most from an expert system because there is no current integration of the hospital data system into the HIV disease management program.

What followed was a literature review of the hospital diagnoses that the HIV expert system would be focusing on (Kaposi's Sarcoma and Cytomegalovirus) to get a complete understanding of the disease and treatment. This was essential to ensure that when the rules are being coded, the correct checks and actions are in place. Because the author is a pharmacist and wanted to test how well she could "wear" both the knowledge expert and database developer "hat", the author did the rule creation on her own. As the result shows that rules were not created 100% correct, in retrospect she should have had a clinical expert review it before the experiment stage.

Creating the relations with the relevant attributes and ensuring the relations are correctly linked took some time. The most difficult part however was the actual rule processing, as a purely SQL approach was developed for inference. On the development side, the last phase was the creation of the prototype website which was needed as a place for users to check rules processing.
Finally the expert system was ready for testing and specific evaluation goals decided. Results of the tests were a questionnaire completed by users, observation of users and tests scenarios completed by users. The latter was done in 2 modes: (1) in manual mode where users evaluated hospital data manually and (2) in automated mode where users evaluated hospital data using recommendations from the *HIV-expert system*. The time and accuracy in (1) and (2) were compared.

7.2 Findings

In the HIV DMP that was reviewed as part of this thesis, clinical experts currently manually adjudicate hospital data. This is both time consuming and not the most efficient use of highly-skilled resources. This thesis evaluates the electronic adjudication of hospital data for HIV patients using an expert system. Expert systems can be a valuable tool in our response to the HIV epidemic.

The aim of this thesis was to develop a solution that can do the electronic adjudication of hospital data. The *HIV-expert system* was developed, implemented and then evaluated.
The clinical experts found the rules were correct for a sample of 20 patients. Automated mode was 53% faster than manual mode. Manual mode had an accuracy of 92% while the automated mode had accuracy of 100%. In the evaluation of whether rule adjudication can be used with confidence in real patients, the main finding was that there is agreement from all users on this. The fact that there is improved efficiency and accuracy when rule adjudication is done in the automated mode verifies the fact that there is improvement in clinical intervention when rule adjudication in automated mode is used. Expert users found the new rule creation spreadsheet usable and adjudication using rules they entered were correct.

In summary, the finding from the experiment showed that adjudication in automated mode was advantageous based on time and accuracy and the new rule creation process was successful.

7.3 Recommendations for future work

For the purposes of this thesis, the author has tried to keep the expert system design as simple as possible by focussing on only the core criteria that needs to be checked. When the expert system is applied in the real world, more extensive checks can be implemented such as checking: specific ART and Chemotherapy/Antiviral therapy drug interactions, latest pathology results and latest claims information. These checks will make the *HIV-expert system* more intelligent which is a goal that is constantly strived for.

During the experiment, it was discovered that in the test scenarios the patient and meds relations lacked additional attributes which, while not impeding the process, would have been useful when following the actions recommended by the system. An example is to indicate whether the patient is pregnant or not. Also from the experiment section, it was found that future work on the *HIV-expert system* is that the URL for the resources used should be included on the user interface.

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Appendix 1 – Database diagram for the *HIV-expert system*

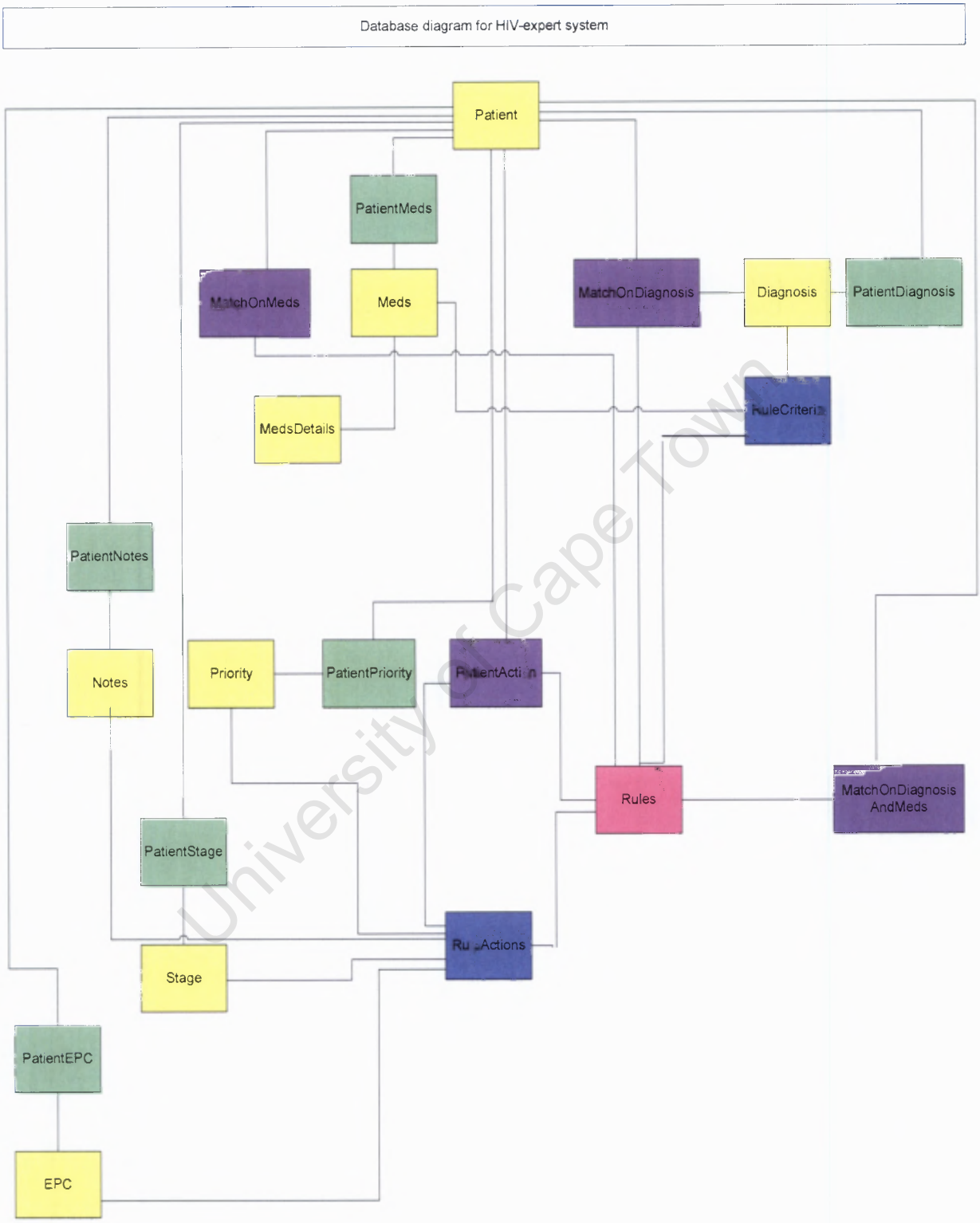


Figure 26: Database diagram of *HIV-expert system*

Appendix 2 – Data dictionary for the *HIV-expert system*

Relation	Description		Attributes	Constraint	Datatype	Allow
Patient	Relation contains all the patient (demographic) information	Each patient record has only 1 record in this relation.	PatientID	Primary Key	Int	Not null
			Title		Varchar(10)	Not null
			FirstName		Varchar(60)	Not null
			Surname		Varchar(60)	Not null
			IDNumber		Varchar(13)	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
Diagnosis	Relation contains hospital diagnosis information	Each diagnosis record has only 1 record in this relation.	DiagnosisID	Primary key	Int	Not null
			DiagnosisName		Varchar(60)	Not null
			ClinicalCode		Varchar(60)	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientDiagnosis	Relation contains specific hospital diagnosis information about the patient that is important to the HIV disease management program (DMP). It links a DiagnosisID to a PatientID.	For every 1 patient record, there can be null or one or many records in this relation. A current record has a ValidTo attribute of null. History exists on this relation which is identified by the ValidTo attribute being populated. The ProcessedDate attribute in this relation refers to the date the record was processed by the *HIV-Expert system*. The InterventionDate attribute in this relation refers to the date the record was intervened on by a pharmacist.	PatientDiagnosisID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			DiagnosisID	Foreign key to DiagnosisID on Diagnosis relation	Int	Not null
			HospitalName		Varchar(60)	Null
			DoctorName		Varchar(60)	Null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
			ProcessedDate		DateTime	Null
			InterventionDate		DateTime	Null

Relation	Description		Attributes	Constraint	Datatype	Allow
Meds	Relation contains basic medication information	Each meds record has only 1 record in this relation.	MedsID	Primary Key	Int	Not null
			MedsType		Varchar(60)	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
MedsDetails	Relation contains more details medication information	For every 1 meds record, there is at least one or can be many records in this relation.	MedsDetailsID	Primary Key	Int	Not null
			MedsID	Foreign key to MedsID on Meds relation	Int	Not null
			MedsType	Foreign key to MedsTypeID on Meds relation	Varchar(60)	Not null
			MedsGroup		Varchar(60)	Null
			MedsGenericName		Varchar(60)	Null
			MedsAbbreviation		Varchar(10)	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientMeds	Relation contains specific medication information that is authorized for a patient on the HIV DMP.	For every 1 patient record, there can be null or one or many records in this relation. A current record has a ValidTo attribute of null. History exists on this relation which is identified by the ValidTo attribute being populated.	PatientMedsID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			MedsID	Foreign key to MedsID on Meds relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null

Relation	Description		Attributes	Constraint	Datatype	Allow
EPC	Relation contains Electronic Processing Code (EPC) information	Each EPC record has only 1 record in this relation.	EPCID	Primary Key	Int	Not null
			EPCDescription		Varchar(100)	Not null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientEPC	Relation contains specific EPC information about the patient that is important to the HIV DMP. It links an EPCID to a PatientID.	For every 1 patient record, there is only 1 current record in this relation. A current record has a ValidTo attribute of null. History exists on this relation which is identified by the ValidTo attribute being populated.	PatientEPCID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			EPCID	Foreign key to EPCID on EPC relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
Notes	Relation contains notes information	Each notes record has only 1 record in this relation.	NoteID	Primary Key	Int	Not null
			NotesText		Varchar(2000)	Not null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientNotes	Relation contains specific Notes information about the patient that is important to the HIV DMP. It links a NoteID to a Patient ID.	For every 1 patient record, there is at least or can be many records in this relation. A current record has a ValidTo attribute of null. History exists on this relation which is identified by the ValidTo attribute being populated.	PatientNotesID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			NoteID	Foreign key to NoteID on Notes relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null

Relation	Description		Attributes	Constraint	Datatype	Allow
Stage	Relation contains stage information	Each stage record has only 1 record in this relation.	StageID			
			StageDescription			
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientStage	Relation contains specific stage information about the patient that is important to the HIV DMP. It links a StageID to a PatientID.	For every 1 patient record, there is only 1 current record in this relation. A current record has a ValidTill attribute date of null. History exists on this relation which is identified with ValidTill attribute populated with a date.	PatientStageID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			StageID	Foreign key to StageID on Stage relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
Priority	Relation contains priority information	Each priority record has only 1 record in this relation.	PriorityID	Primary Key	Int	Not null
			PriorityDescription		Varchar(60)	Not null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
PatientPriority	Relation contains specific Priority information about the patient that is important to the HIV DMP. It links a PriorityID to a PatientID.	For every 1 patient record, there is only 1 current record in this relation. A current record has a ValidTill attribute of null. History exists on this relation which is identified with ValidTill attribute populated with a date.	PatientPriorityID	Primary Key	Int	Not null
			PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			PriorityID	Foreign key to PriorityID on Priority relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null

Relation	Description		Attributes	Constraint	Datatype	Allow
Rules	Relation contains a list of rules that are coded for rule processing	The relation contains a list of rules that are coded for rule processing. The NumberOfDiagnosis attribute on this relation refers to the number of diagnosis criteria that need to be met for this rule to be met. Similarly, the NumberOfMeds attribute on this relation refers to the number of meds criteria that need to be met for this rule to be met.	RuleID	Primary Key	Int	Not null
			RuleName		Varchar(60)	Not null
			NumberOfDiagnosis		Int	Not null
			NumberOfMeds		Int	Not null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
RuleCriteria	Relation contains the list criteria that need to be met for a rule to be passed	For every 1 rule record, there is at least 1 rule criteria in this relation.	RuleCriteriaID	Primary Key	Int	Not Null
			RuleID	Foreign key to RuleID on Rules relation	Int	Not Null
			DiagnosisID	Foreign key to DiagnosisID on Diagnosis relation	Int	Not Null
			MedsID	Foreign key to MedsID on Meds relation	Int	Not Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null

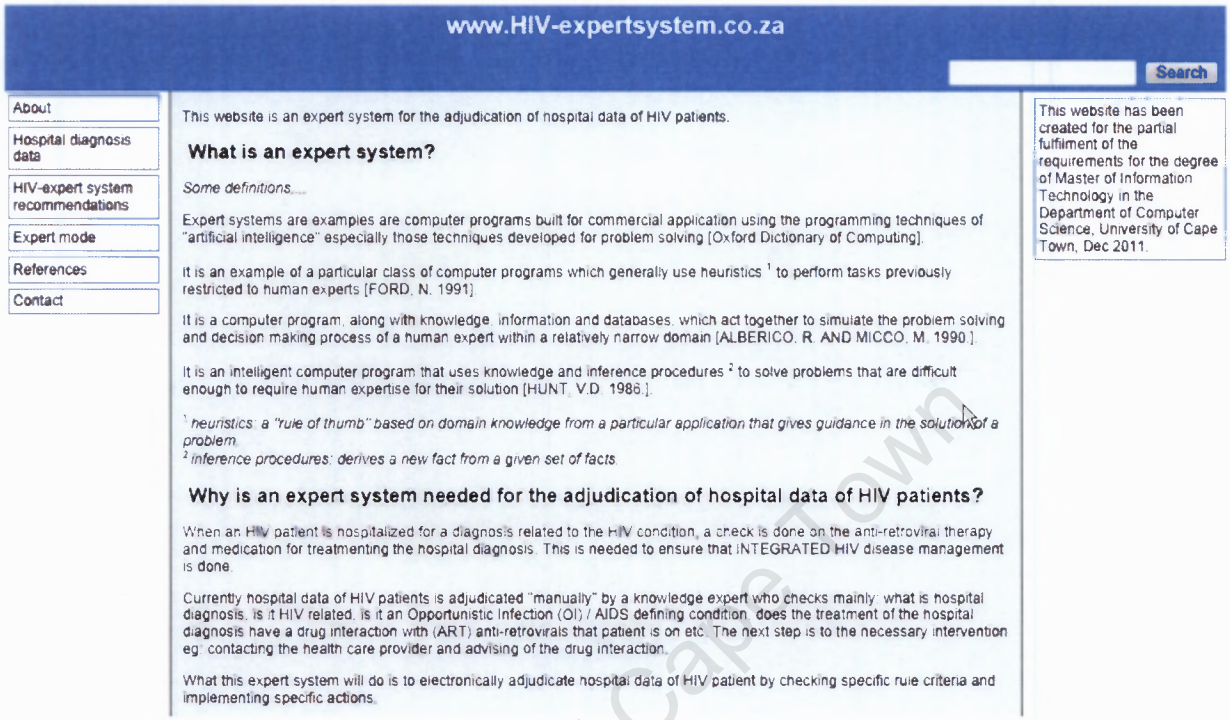
Relation	Description		Attributes	Constraint	Datatype	Allow
RuleActions	Relation contains the list actions that can be applied to a patient record once it has passed all the criteria a rule.	For every 1 rule record, there is at least 1 rule action in this relation.	RuleActionID	Primary Key	Int	Not Null
			RuleID	Foreign key to RuleID on Rules relation	Int	Not Null
			Action		Varchar(60	Not null
			NoteID	Foreign key to NoteID on Notes relation	Int	Not Null
			EPCID	Foreign key to EPCID on EPC relation	Int	Not Null
			StageID	Foreign key to StageID on Stage relation	Int	Not Null
			PriorityID	Foreign key to PriorityID on Priority relation	Int	Not Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
MatchOnDiagnosis	Relation contains the list of patient record that match the rule criteria based on diagnosis	For every 1 patient record and rule record combination, there is can be null or many records in this relation	PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			RuleID	Foreign key to RuleID on Rules relation	Int	Not null
			DiagnosisID	Foreign key to DiagnosisID on Diagnosis relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null

Relation	Description		Attributes	Constraint	Datatype	Allow
MatchOnMeds	Relation contains the list of patient record that match the rule criteria based on meds	For every 1 patient record and rule record combination, there is can be null or many records in this relation	PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			RuleID	Foreign key to RuleID on Rules relation	Int	Not null
			MedsID	Foreign key to MedsID on Meds relation	Int	Not null
			ValidFrom		DateTime	Null
			ValidTo		DateTime	Null
			CreatedUser		Varchar(60)	Null
			CreatedDate		DateTime	Null
			ModifiedUser		Varchar(60)	Null
			ModifiedDate		DateTime	Null
MatchOnDiagnosisAndMeds	Relation contains the list of patient record that match the rule criteria based on diagnosis AND meds	For every 1 patient record and rule record combination, there is can be null or1 record in this relation	PatientID	Foreign key to PatientID on Patient relation	Int	Not null
			RuleID	Foreign key to RuleID on Rules relation	Int	Not null
PatientAction	Relation contains the list of patient record that match the rule and will have the rule actions executed	For every 1 patient record and rule record combination, there is can be null or1 record in this relation	PatientID	Foreign key to PatientID on Patient relation	Int	Null
			RuleID	Foreign key to RuleID on Rules relation	Int	Null
			RuleActionID	Foreign key to RuleActionID on RuleAction relation	Int	Null
			Action		Varchar(60)	Null
			ActionPriority		Int	Null

Table 16: Data dictionary for *HIV-expert system* database

Appendix 3 - Prototype website details

Home page



Expert mode

Step 1: Select "Expert mode" from the menu on the left-hand side of the home page

Step 2: Select "Query Patient records by clicking on the hyperlink

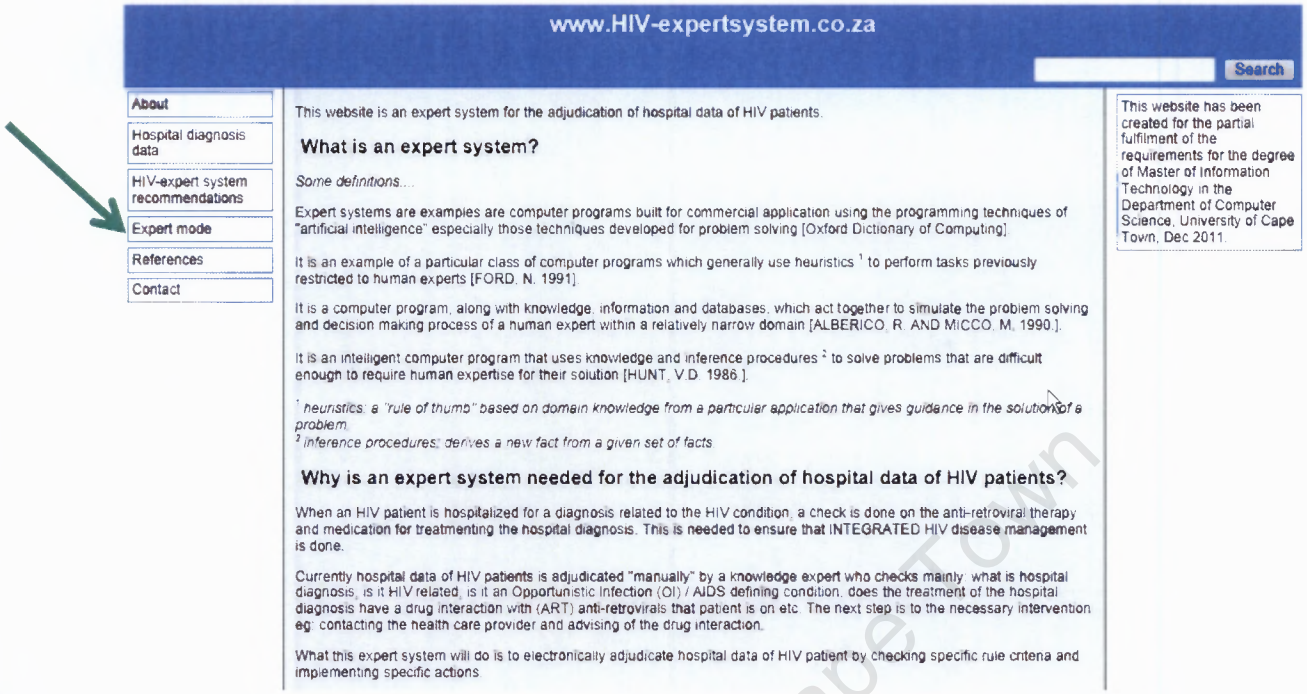
Step 3: Click 'execute"

The Patient Details Query SQL Response page will be displayed.

PatientID	Title	FirstName	Surname	IDNumber
1000	Mr	Donald	Duck	7310060178089
1001	Mrs	Dippy	Duck	7210060178089
1002	Mr	Mickey	Mouse	7110060178089
1003	Mrs	Minnie	Mouse	7010060178089
1004	Mr	Bart	Simpson	6910060178089
1005	Miss	Lisa	Simpson	6810060178089
1006	Mr	Ben	Ten	6710060178089
1007	Mr	Peter	Pan	6610060178089
1008	Mr	Peter	Rabbit	6510060178089
1009	Mr	Benjamin	Bunny	6410060178089
1010	Mr	Cotton	Tail	6310060178089
1011	Mrs	Squirrel	Nutkin	7310060178089
1012	Mr	Tom	Kitten	7210060178089
1013	Mr	Gland	Bland	7110060178089
1014	Mr	Samuel	Whiskers	7010060178089
1015	Mr	Jeremy	Fisher	6910060178089

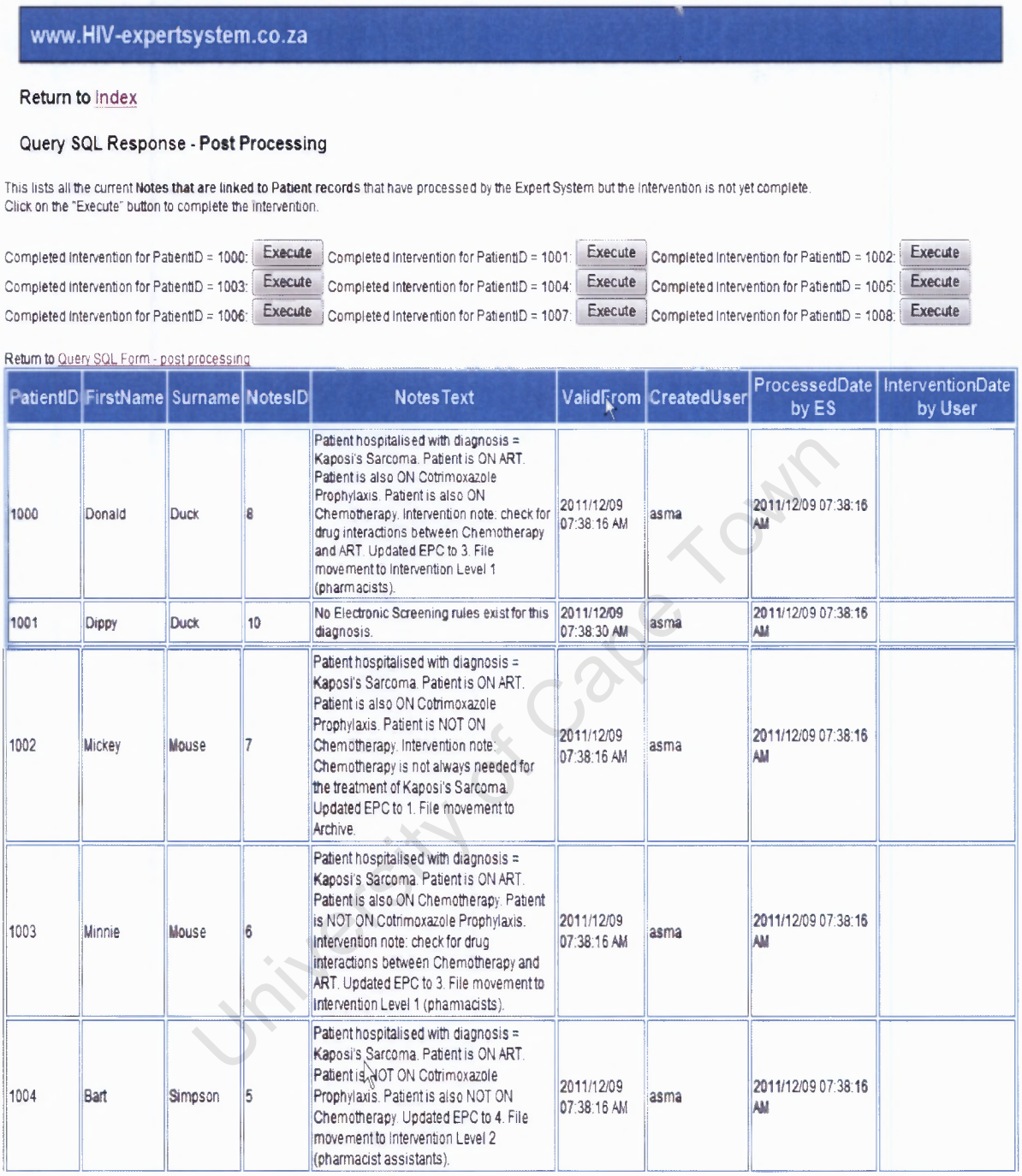
HIV-expert system recommendations

Step 1: Select "Expert mode" from the menu on the left-hand side



Step 2: Select "Query Patient Notes records by clicking on the hyperlink

The Patient Notes Query SQL Response – Post Processing Form page will be displayed.



www.HIV-expertsystem.co.za

Return to Index

Query SQL Response - **Post Processing**

This lists all the current **Notes that are linked to Patient records** that have processed by the Expert System but the intervention is not yet complete.
Click on the "Execute" button to complete the intervention.

Completed Intervention for PatientID = 1000: Execute | Completed Intervention for PatientID = 1001: Execute | Completed Intervention for PatientID = 1002: Execute
Completed Intervention for PatientID = 1003: Execute | Completed Intervention for PatientID = 1004: Execute | Completed Intervention for PatientID = 1005: Execute
Completed Intervention for PatientID = 1006: Execute | Completed Intervention for PatientID = 1007: Execute | Completed Intervention for PatientID = 1008: Execute

Return to Query SQL Form - post processing

PatientID	FirstName	Surname	NotesID	NotesText	ValidFrom	CreatedUser	ProcessedDate by ES	InterventionDate by User
1000	Donald	Duck	8	Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is also ON Cotrimoxazole Prophylaxis. Patient is also ON Chemotherapy. Intervention note: check for drug interactions between Chemotherapy and ART. Updated EPC to 3. File movement to Intervention Level 1 (pharmacists).	2011/12/09 07:38:16 AM	asma	2011/12/09 07:38:16 AM	
1001	Dippy	Duck	10	No Electronic Screening rules exist for this diagnosis.	2011/12/09 07:38:30 AM	asma	2011/12/09 07:38:16 AM	
1002	Mickey	Mouse	7	Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is also ON Cotrimoxazole Prophylaxis. Patient is NOT ON Chemotherapy. Intervention note: Chemotherapy is not always needed for the treatment of Kaposi's Sarcoma. Updated EPC to 1. File movement to Archive.	2011/12/09 07:38:16 AM	asma	2011/12/09 07:38:16 AM	
1003	Minnie	Mouse	6	Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is also ON Chemotherapy. Patient is NOT ON Cotrimoxazole Prophylaxis. Intervention note: check for drug interactions between Chemotherapy and ART. Updated EPC to 3. File movement to Intervention Level 1 (pharmacists).	2011/12/09 07:38:16 AM	asma	2011/12/09 07:38:16 AM	
1004	Bart	Simpson	5	Patient hospitalised with diagnosis = Kaposi's Sarcoma. Patient is ON ART. Patient is NOT ON Cotrimoxazole Prophylaxis. Patient is also NOT ON Chemotherapy. Updated EPC to 4. File movement to Intervention Level 2 (pharmacist assistants).	2011/12/09 07:38:16 AM	asma	2011/12/09 07:38:16 AM	

The details listed in the "NotesText" column are the recommendations for the intervention plan from the *HIV-expert system* after processing this specific patient record.
Once the actual intervention has been done by contacting the Dr, the user will the click the execute button next to the specific PatientID at the top of the screen.
This will then insert an "InterventionDate" into the PatientDiagnosis relations and remove the patient from the display on this page. This is because this page only displays the current cases that need intervention.

Website construction – sample code

HTML

SQL_query_button1_VB.html

```
<html lang="en">
    <head>
        <meta charset="utf-8" />
        <title>SQL Query Entry Form</title>
            <link rel="stylesheet" href="1_Column_layout.css" type="text/css""/>

    </head>
    <body>

        <div id="container">
            <H1>www.HIV-expertsystem.co.za</H1>

            <H2> Return to <a href="Index.html">Index</a>  </H2>

            <H2>Query SQL Form</H2>         <!--Query SQL form -->


                <br/>

                <p>

                <description>
                    This is a list of Query records in the database:     <!-- List of Query SQL forms below as hyperlinks -->

                    Click on the hyperlink to display details.
                </description>

```

ASP

```
    <description>This is a list of current <b>Notes</b> details. </description>

    <p></p>

     <table border="1" width="100%">          <!-- table for output with headings -->
        <tr>
            <th>NotesID</th>
            <th>NotesText</th>
        </tr>
    <%
    'Declare dimension variables
    DIM objConn, connectionString, sql_query_button10, Rs, intRecordsAffected

    '''To get data from database follow these steps
    '''1. Create ADODB.Connection object, set connection string and open connection
    '''2.Create ADODB.Recordset object to store the sql query results. e.g. Set objRS = objConn.Execute(your sql statement,noofrecordsaffected)
    '''3. Iterate thru your recordset and write out results as desired on screen/browser

    'Create an instance of the record set = Rs and connection objects through ADO
    connectionString = "Provider=SQLOLEDB.1;Persist Security Info=False;User ID=hivexpay_dbuser;Password=cezhzNuU;Initial Catalog=hivexpay_hiv-
    Set objConn = Server.CreateObject("ADODB.Connection")
        objConn.ConnectionString = connectionString

        objConn.Open
        sql_query_button10= "EXEC q_Notes"            'SQL query details here. sql_query_button6 = SELECT *
        Set Rs = Server.CreateObject("ADODB.Recordset")
        Set Rs = objConn.Execute(sql_query_button10,intRecordsAffected)

        if intRecordsAffected < 0 then              'if 1 = if number of records < 0     then move first
            Rs.MoveFirst
        end if                                      'end if 1
    %>
```

External style sheets

```
.ruleMenu
    {
        z-index: 99;
        display:none;
        position:absolute;
        top: 100px;
        left: 70px;
        background-color: CornFlowerBlue;
        border: solid 1px #000000; padding: 5px;
        color: #FFFFFF;
    }

.ruleMenu a
    {
        color: #FFFFFF;
    }
```

Appendix 4 - Survey question screen prints

Question 1: Evaluation of rules

Rule Name	Question 1: Is the rule set up correct for existing rules? Prior to implementation, does a clinical expert need to check the rules to be applied by the expert system? Post implementation, does a "human" user need to check each record processed by the rules in the expert system?	Evaluation			
Karposi's Sarcoma Rule 1 to 8	1a.1 The rules are perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.2 The rules have some major errors e.g. rule recommendation incorrect	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.3 The rules have some minor errors e.g. text changes to notes	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.4 The rules are perfectly complete e.g. no missing criteria	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.5 The rules are clear, concise, unambiguous and understandable	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.6 The rules are perfectly consistent and do not conflict with each other	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.7. Prior to implementation, the rules do not have to be checked by a clinical expert. The rules can be applied as is.	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
	1a.8. Once the rules have been checked by clinical expert, the rules are usable and perfectly safe to apply in practice. Post implementation, a "human" user does not need to check each record processed by the rules in the expert system. I have complete confidence in the application of the rules in practice.	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree

Question 2: Evaluation of rules adjudication

Question 2a

Patient ID	Question 2a: Is the rule adjudication in automated mode correct for a sample of patients (20 patients)?	Evaluation			
Patient ID = 1000	2a.1 The rule adjudication for Patient ID = 1000 is perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
...					
Patient ID = 1030	2a.1 The rule adjudication for Patient ID = 1030 is perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree

Question 2b

In this section, only 1 response is illustrated

Patient ID	Question 2b: Is the rule adjudication in automated mode faster than manual mode for a sample of patient (20 patients)?	Time taken in Manual mode	Time taken in Automated mode
Patient ID = 1000	2b.1 The rule adjudication time for Patient ID = 1000 per mode was as follows:		

Question 2c

Patient ID	Question 2c: Is the rule adjudication in automated mode more accurate than rule adjudication in manual mode for a sample of patient (20 patients)?	Evaluation			
Patient ID = 1000	2c.1 The rule adjudication in manual mode for Patient ID = 1000 had an accuracy of:	☐ 100%	☐ 90% to 99%	☐ 80% to 89%	☐ 70% to 79%
Patient ID = 1001	2c.1 The rule adjudication in manual mode for Patient ID = 1001 had an accuracy of:	☐ 100%	☐ 90% to 99%	☐ 80% to 89%	☐ 70% to 79%
Patient ID = 1002	2c.1 The rule adjudication in manual mode for Patient ID = 1002 had an accuracy of:	☐ 100%	☐ 90% to 99%	☐ 80% to 89%	☐ 70% to 79%
Patient ID = 1003	2c.1 The rule adjudication in manual mode for Patient ID = 1003 had an accuracy of:	☐ 100%	☐ 90% to 99%	☐ 80% to 89%	☐ 70% to 79%
Patient ID = 1004	2c.1 The rule adjudication in manual mode for Patient ID = 1004 had an accuracy of:	☐ 100%	☐ 90% to 99%	☐ 80% to 89%	☐ 70% to 79%

Question 2d

Question 2d: Refer to answers in question 2a, 2b and 2c. Would the rule adjudication be used with confidence on real patients? Does it improve clinical intervention?	Evaluation			
2d.1 Does the rules adjudication save time	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
2d.2 Is the rules adjudication more accurate	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
2d.3 Is the rules adjudication usable and perfectly safe to apply in practice. I have complete confidence in their application	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
2d.4 If the rules adjudication is NOT usable and NOT perfectly safe to apply in practice. What needs to be changed?	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree

Question 3a

Question 3a: Is the new rule creation spreadsheet usable?	Evaluation			
3a.1. New rules information was entered on a spreadsheet. Was the information requested clear, concise, unambiguous and understandable	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree

Question 3b

Question 3b: Is the rule adjudication using the new rule correct for a sample of patients (3 patients)?	Evaluation			
3b.1 The rule adjudication for Patient ID = 1040 is perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
3b.2 The rule adjudication for Patient ID = 1041 is perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
3b.3 The rule adjudication for Patient ID = 1042 is perfectly correct i.e. the recommendations are as expected	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
3b.4 The new rules loaded had some major errors	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree
3b.5 The new rules loaded in the database had some minor errors	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree

Question 3c

Question 3c: Is the new rule creation process usable?	Evaluation			
3c.1 Based on the answers in question 3a and 3b, the rules adjudication are usable and perfectly safe to apply in practice. I have complete confidence in their application	☐ Strongly agree	☐ Agree	☐ Disagree	☐ Strongly disagree