Ruprecht-Karls-Universität Heidelberg - Hochschule Heilbronn

Master-Thesis

Extenting a hostpital information system with a clinical decision support system for drug interactions

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Abstract

There are many drug interactions and to know every single interaction is impossible. In Uganda, a country located in East Africa, patients often do not get a patient information leaflet when a physician prescribes drugs because they only get the drugs without packaging and information inside. Even in developed countries many poeple die because of drug interactions.

This work aims at developing a clinical decision support system for different kinds of drug interactions: 1) drug-drug interaction, 2) drug-food interactions, 3) drug-condition interactions and 4) drug-disease interactions. This system must be integrated into an existing hospital information system called electronic Health Management Information System (eHMIS).

In the first part of this thesis different kinds of clinical decision support systems are described to find out which one is the best for eHMIS. The two different types are knowledge-based and non knowledge-based systems.

The second part of this thesis, the data base of eHMIS is extended to have a full knowledge base for the new module which contains drug-drug interactions, drug-food interactions, drug-disease interactions as well as drug-condition interactions. Therefore new tables were created and filled with data of several data bases with drug interactions.

The last part is about designing the clinical decision support system for drug interactions with the knowledge base of eHMIS, including the implementation considering the integration into the existing system. To know how health professionals in Uganda work with an electronic health system as well as their other workflows was important. The system now runs in a hospital in Kampala, the capital of Uganda and in a health center level three in Mifumi, a village located in the east of the country.

Declaration of Authenticity

I have written this thesis independently, solely based on the literature and tools mentioned in the chapters and the appendix. This document - in the current or a similar form - has not and will not be submitted to any other institution apart from the University of Heidelberg and University of Applied Science Heilbronn to receive an academical grade.

Heiko Ströhle

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1 Introduction

1.1 Motivation

In most developing countries health information management is realized paper-based. In Uganda, a country located in East-Africa, there is also the same situation but electronical systems were and will be implemented in hospitals and health professionals currently get an induction into it. The paper-based system is comprised of data-set formats and is called Health Management Information System (HMIS). However, with a non-electronical HMIS it is time-consuming and more expensive, because more health professionals are needed. There can be also errors while recording data and transferring it to paper forms. For example a health worker is writing 57 kilograms for body weight instead of 75 kg. The body weight can affect dosages of medication so it is important to know the correct weight. To avoid such errors Electronic Health Record (EHR) can assist health professionals recording patient data correctly by flag abnormal values[37] or provide lists of possible explanations for those abnormalities[25].

To support physicians and other health workers in their decisions an eletronical health management information system is a good choice. Such an information system has several advantages: 1) improve quality and convenience of patient care, 2) increase patient participation in their care, 3) improve accurace of diagnoses and health outcomes, 4) improve care coordination, 5) increase practice efficiencies and cost saving[37].

In Uganda an electronical version of a HMIS is called eHMIS[19]. eHMIS were developed by Dr. Simon Ndira as part of his PhD. programme. It provides modules for several wards in a hospital like Mengo Hospital in Kampala but there is no decision support system which shows alerts if two drugs a patient is taken interact. Such interactions can causes fatal consequences like death [16]. An underestimated problem is also a drug-to-food intaction like antibiotic and milk [21]. Especially a hospitals Outpatient department (OPD) has a high workload with patients and medication. A clinical decision support systems may help doctors to improve treatments of patients through assisting them in their decision making. You can also support patients directly with free guides like *A Guide from the National Consumers League and U.S. Food and Drug Administration*[27]. But people in delevoping countries do not have good internet access or the education is too low to know about guides or articles. That is why health professionals need to support patients by saying how to use medication and explain possible interactions.

In developing countries further problems like missing technical resources or power

breakdowns complicate the deployment and usage of a drug-to-X system which alerts physicians if there is a bad interaction.

Risks with drugs do not mostly result of individually misconduct but of suboptimal procedures of medication processes. Therefore it is important, all health professionals need to work together to minimize risks[42].
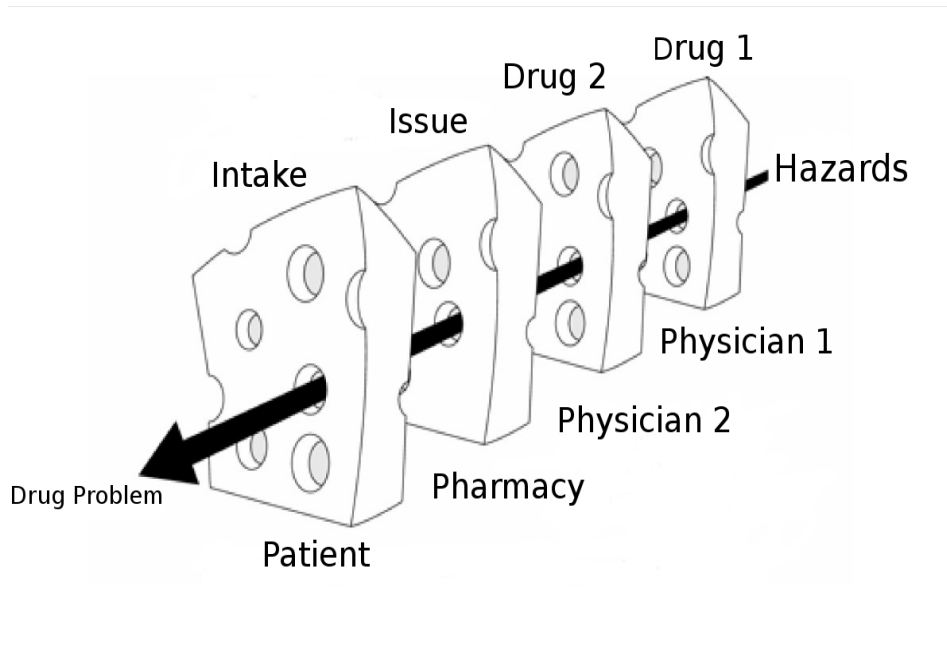
Figure 1.1: The swiss cheese model by Reason shows, how a medication error can emerge if safety barries fail.

1.2 Types of drug interactions with examples

The idea was to implement a system for drug interactions for different areas, which are described later in the following sections. Generally a drug interaction means a situation in which an ingredient or a substance influences the activity of another substance. There are three possible actions: first a synergestic (the effect of a drug increases) or an antagonistic (drug's effect decreases) or a substance of a drug produces a new effect.

1.2.1 Drug-drug interactions

A drug to drug interaction occurs if a person is taking more than one drug and one or more of the taken drugs interact with a substance of another taken drug. Most adverse drug to drug interactions are either pharmacodynamic or pharmacokinetic in nature.

To describe these it goes beyond the scope of this thesis. The following list shows some drug-drug interactions[8][31][6]:

- *Pain relievers*

  - **Tylenol (acetaminophen) and Rifadin, Rimactane (antibiotics rifampin):**
    Gets in the way of how the liver processes acetaminophen and increases the risk of liver problems when taking acetaminophen.

  - **Aspirin and Diabinese (chlorpropamide):**
    Aspirin increases the bloodsugar-lowering effects of diabetes medicines.

  - **Aspirin and Anti-seizure drugs like Dilantin and valproic acid like Depakene:**
    Aspirin gets in the way of the anti-seizure drugs binding with proteins in the blood and leads to increased anti-seizure drug levels in your blood.

  - **Aspirin and Ibuprofen 200:**
    Ibuprofen may reduce the effectiveness of aspirin if you are taking it to prevent heart attacks or strokes. This interacion also can developing gastrointestinal ulcers and bleeding.

  - **Paracetamol and Emla (lodicaine/prilocaine topical):**
    "Prilocaine topical can cause a condition called methemoglobinemia that reduces the oxygen-carrying capacity of the blood to different organs, and combining the medication with acetaminophen may increase the risk. Infants and patients with certain conditions such as glucose-6-phosphate dehydrogenase deficiency or anemia are more likely to develop this condition. You should seek immediate medical attention if you notice signs and symptoms such as a gray discoloration of the skin, mouth, or nail bed; nausea; headache; dizziness; lightheadedness; fatigue; shortness of breath; rapid or shallow breathing; a rapid heartbeat; anxiety; and confusion."

- *Antihistamines*

  - **Dimetapp Allergy (brompheniramine) and Qsymia (phentermine/ topiramate):**
    Topiramate are for increasing the body temperature and decreasing sweating. Combined with a brompheniramine like Dimetapp the effects can be greater. Other adverse effects could be heat stroke and hospitalization in some people. Also dizziness, lightheadedness or drowsiness may occur.

  - **Epiklor (potassium chloride) and Dramamine (dimenhydrinate):**
    "The following interaction applies only if you are taking potassium in a solid formulation (i.e., tablet or capsule swallowed whole): Talk to your doctor before using potassium oral tablets or capsules together with CS2. Depending

on the dose of CS2 and your overall physical health, combining these medications may increase the irritant effects of potassium on your stomach and upper intestine. This can rarely result in ulcers, bleeding, and other gastrointestinal injury." Also occur can abdominal pain, bloating, sudden diziness or lightheadedness, nausea, vomiting (with blood), loss of appetite and much more.

- *Descongestants*

  - **Sudafed Congestion (pseudoephedrine) and Atapryl (selegiline):**
    "Using selegiline together with pseudoephedrine is not recommended. Combining these medications can cause dangerously high blood pressure and even death. You may use pseudoephedrine only after you have been off selegiline for at least 14 days. You should seek immediate medical attention if you experience sudden and severe headache, blurred vision, confusion, seizures, chest pain, nausea or vomiting, sudden numbness or weakness (especially on one side of the body), speech difficulties, fever, sweating, lightheadedness, and/or fainting during treatment with selegiline, as these may be signs and symptoms of excessively high blood pressure. "

  - **Contact Cold and Sore Throat (pseudophedrine) and Cymbalta (duloxetine):**
    "Combining these medications can increase the risk of a rare but serious condition called the serotonin syndrome, which may include symptoms such as confusion, hallucination, seizure, extreme changes in blood pressure, increased heart rate, fever, excessive sweating, shivering or shaking, blurred vision, muscle spasm or stiffness, tremor, incoordination, stomach cramp, nausea, vomiting, and diarrhea. You should contact your doctor immediately if you experience these symptoms while taking the medications. It is important to tell your doctor about all other medications you use, including vitamins and herbs. "

- *Cough Medicines*

  - **Delsym (dextromethorphan) and Celexa (citalopram):**
    "Combining these medications can increase the risk of a rare but serious condition called the serotonin syndrome, which may include symptoms such as confusion, hallucination, seizure, extreme changes in blood pressure, increased heart rate, fever, excessive sweating, shivering or shaking, blurred vision, muscle spasm or stiffness, tremor, incoordination, stomach cramp, nausea, vomiting, and diarrhea. You should contact your doctor immediately if you experience these symptoms while taking the medications. It is important to tell your doctor about all other medications you use, including vitamins and herbs. "

1.2.2 Drug-food interactions

A drug to food interaction occurs if a person is eating certain food and taking one or more drugs. Thereby, it is possible that the effect increases, decreases or an unexpected effect appears. The list below shows some of them[8][31][6]:

- **Grapefruit juice and certain blood pressure-lowering drugs:**
  "Grapefruit juice is often mentioned as a product that can interact negatively with drugs, but the actual number of drugs the juice can interact with is less well-known. Grapefruit juice shouldn't be taken with certain blood pressure-lowering drugs or cyclosporine for the prevention of organ transplant rejection. That's because grapefruit juice can cause higher levels of those medicines in your body, making it more likely that you will have side effects from the medicine. The juice can also interact to cause higher blood levels of the anti-anxiety medicine Buspar (buspirone); the anti-malaria drugs Quinerva or Quinite (quinine); and Halcion (triazolam), a medication used to treat insomnia. "

- **Alcohol and drugs:**
  The patient information leaflet and every physician says that alcohol can influences the effects of drugs. Trinking alcohol and alcohol abuse may change the amount of enzymes in the liver, above all the enzyme CYP2E1. *"Cytochrome P450 2E1 (abbreviated CYP2E1, EC 1.14.13.n7), a member of the cytochrome P450 mixed-function oxidase system, is involved in the metabolism of xenobiotics in the body. In humans, the CYP2E1 enzyme is encoded by the CYP2E1 gene.[1] While it is involved in the oxidative metabolism of a small range of substrates (mostly small polar molecules), there are many important drug interactions mediated by CYP2E1."*[?]

- **Vitamin E and blood-thinning medication:**
  "Taking vitamin E with a blood-thinning medication such as Coumadin can increase anti-clotting activity and may cause an increased risk of bleeding. "

1.2.3 Drug-condition interactions

If a person is in a specific condition, for example pregnant or underweight. It may occur when an existing medical condition makes certain drugs potentially harmful.

"Animal studies failed to reveal embryotoxicity or teratogenicity, although maternal toxicity in some animal studies resulted in increased incidence of abortion. There are no controlled data in human pregnancy. However, ciprofloxacin has been shown to distribute into amniotic fluid. Concentrations reported were 57% (at 2 to 4 hours post dose) to 1000% (at 10 to 12 hours post dose) of that found in maternal serum. A review by the Teratogen Information System concluded that a substantial risk is unlikely; however, there were insufficient data to state that there is no risk. Cartilage damage and arthropathies associated with ciprofloxacin have been reported in immature animals

of various species, giving rise to concern over its possible toxic effects on human fetal bone formation. Because safer alternatives are generally available, some experts consider ciprofloxacin contraindicated during pregnancy, especially during the first trimester. Of 549 cases reported by the European Network of Teratology Information Services involving fluoroquinolone exposure (including ciprofloxacin), congenital malformations were reported in 4.8%; however, this was not higher than the background rate. In the U.S. Michigan Medicaid surveillance study of 229,101 pregnancies, major birth defects were reported in 3 of 132 exposed neonates. An association between ciprofloxacin and congenital defects is not supported by these data. Berkovitch and colleagues reviewed 35 pregnancies in women who received norfloxacin or ciprofloxacin during the first trimester for urinary tract infection. No malformations were observed among the infants of these women. There were no joint problems or walking delays, and when compared to non-exposed infants, there was no apparent difference in the acquisition of milestones. In mass casualty settings after release of biological weapons, the Working Group on Civilian Biodefense has recommended ciprofloxacin as the drug of choice for postexposure prophylaxis and treatment of anthrax, and as an alternative for tularemia and plague. The risk is outweighed by the high fatality rates from these infections. FDA pregnancy category C: Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. "

1.2.4 Drug-disease interactions

This happen when a prescription or over-the-counter medication interacts, or interferes, with a disease or condition that a patient have. For example Non-steroidal anti-infflammatory drugs (NSAID) may have an effect to the blood pressure. People with high blood pressure should not take these drugs.

1.3 Goal of this Work

Extending an existing hospital information system the present thesis following six goals: 1) extent the existing database to have a full knowledge base for a drug interaction system, 2) implement a clinical decision support system for different drug interactions, 3) integrate the new module into eHMIS, 4) studying if such a decision support system is useful and health worker will accept it, 5) assist health professionals in their work by alerting if there is a drug interaction, 6) help patients to avoid drug-food interactions.

1.4 Structure of the Thesis

This thesis is divided in seven chapters and an appendix. After the introduction part in this chapter, the second chapter starts with a describtion of the environment, Uganda's

health system and infrastructure. Futhermore, it describes health facilities in which the system is used, both the non-electronical and electronical health management information system.

The third chapter is about the fundamentals of clinical decision support. How such a system works is the basic explanation of this chapter. It illustrates also a common possibility of a structure of a clinical decision support system, for knowledge- and non-knowledge based.

Chapter four is about how the CDSS was designed and implemented. It illustrates the knowledge base and the written modules of drug interactions. This chapter also contains the technical environment with models and schemes.

The text of the fith chapter lists the results of impolementing the approach of a clinical decision support system for drug interactions.

Chapter six discusses these results and gives an outlook on possible future extensions and improvements.

Finally the appendix contains written functions and the bibliography.

2 Describtion of the environment

The clinical decision support system was integrated into eHMIS [19]. eHMIS is already implemented in some hospitals in Uganda, for example at Mengo Hospital, located in Kampala, the capital of Uganda. It is also installed at Mifumi Health Centre but in another version. Mifumi is a small village based 27km from Tororo town, in Eastern Uganda. Because health care systems and infrastructures of developing countries can differ from systems of developed countries this chapter will deliver an insight into Ugandas health care system and infrastructure. Furthermore a description of Mengo Hospital and eHMIS will be given.

2.1 Ugandas's health system and infrastructure

According to the Ministry of Health (MoH)[24] and Uganda Bureau Of Statistics (UBOS)[39] the health structure of Uganda can be described as follows [28]: There are a total number of 11,130 health facilities in Uganda. 62.3% are owned by the Goverment of Uganda, 19.2% belongs to the private sector and Private Not For Profit (PNFP) own 18.4%. Currently there are two National Referral Hospitals (NRH), twelve Regional Referral Hospitals (RRH) and 135 general hospitals, 56 PNFP hospitals and 9 Private Hospitals (PHP) as well as 1552 health center. Government hospitals are classified by the services they provide. There are:

- NRH. In Uganda there are 2 NRHs: Butabikahospital in Kampala as well as Mulago hospital, also in Kampala. These national refferal hospitals provide both teaching services and health research and specialized services.

- RRH provide specialist services like radiology, high level surgical, psychiatric and more.

- General/District Hospitals provide a large output for outpatient and inpatient services and als provide support supevision to lower level health facilities.

Hospitals are at the top of the healthcare chain. In national referral and regional referral hospitals there are specialits available. District and general hospitals are staffed by general doctors. They are supposed to provide at least the following services: medicine, surgery, paediatrics, obstetrics and gynaecology, dentistry, anaesthesia, radiology, clinical laboratory and community health.

The other categories of health facilities are the Health Centers. They are devided in three grades:

- Health centre 2 (Enrolled Comprehensive Nurse) (HC II): According to the Ugandan government's health policy, every parish is supposed to have one of these centres. A health centre II facility, serving a few thousand people, should be able to treat common diseases like malaria. It is supposed to be led by an enrolled nurse, working with a midwife, It runs an outpatient clinic, treating common diseases and offering antenatal care.

- Health centre 3 (Cinical Officer) (HC III): This facility should be found in every subcounty in Uganda. These centres should have about 18 staff, led by a senior clinical officer, It should also have a functioning laboratory.

- General/District Hospital and Health centre 4 (Medical Officer) (HC IV): This level of health facility serves a county. In addition to services found at health centre III, it should have wards for men, women, and children and should be able to admit patients. It should have a senior medical officer and another doctor as well as a theatre for carrying out emergency operations.

2.1.1 Mengo Hospital

Kampala district has an estimated population of 1.72 million [36]. Kampala district provides 5 hospitals and around 200 health units [28], including Mengo Hospital. Mengo Hospital, also known as Namirembe Hospital, is a Non-Government Hospital. Services provided are: antenatal, counselling and come-care, dental, eye, laboratory and occupational therapy.

2.1.2 Mifumi Health Center

The Mifumi Health Center is a HC III, located 27km from Tororo town in Mifumi, Eastern Uganda. With a hinterland of around 80,000 people, it provides appropriate health care services with a focus on enhancing quality of life and protecting the rights of vulnerable people. Opened in 2001 the main diseases encountered are: Malaria, Malnutrition, HIV, Schistosomiasis and others. There is also a offer for health education, HIV screening and Prevention of Mother to Child Transmission of HIV.

2.2 Health Management Information System: HMIS

The HMIS was released by the Ministry of Health, Replublic of Uganda. It's objective is to provide a routine based system to collect data about the health system. HMIS has

been designed for use of all units and districts for planning and improving the health system of Uganda by evaluating the healthcare system [19].

HMIS consists exclusively of paper-based database formats for all levels of the health system, i.e. forms for the health units, the health sub-districts, the districts and the Ministry of Health Headquarters. Reports are delivered form the lowest level (health units) up to the next level on a monthly basis. The list below shows which data are collected [19]:

- Morbidity data from outpatient departments: These are among others: Mother and Child Health and Family Planning activities, essential drugs, vaccines and contraceptive stock.

- Morbidity and mortality data from inpatient departments: Referrals, number of admissions and deaths by diagnosis, utilization of special services, etc.

- Notifiable diseases

- Epidemiological surveillance reports

The last version implemented both formal and on-the-job training for health workers.

2.3 Electronical version: eHMIS and its platform

As in the above section stated before HMIS documentation was exclusively paper-based. Hence Dr. Simon Peter Ndira designed and developed an electronical version of HMIS called eHMIS (electronical Health Management Information System) as a part of his doctoral thesis. eHMIS enables hospital staff to manage patient data electronically in the health environment[19]. Before the project for a decision suport system started, eHMIS provided several modules for managing patient data for different wards like dental, optics, laboratory or ophthalmology. Other functions like administrate a user profile or a ticketing-system is also available. Users with required permissions are able to carry out functions for system maintenance like for example database dumps. Also permission rights for different users can be managed as well as for user groups.

To run eHMIS, which is browser-based, you need a so called *LAMP* environment. LAMP stands for *Linux, Apache, MySQL and PHP*. In both health facilities Mengo Hospital and Mifumi Health Center the network structure is made up by a client-server-technology. At Mengo Hospital the server is located in the information technology department and at Mifumi Health Center in the pharmacy. Laptops for working are available in every room where they needed.

3 State of the Art

3.1 Fundamentals of Clinical Decision Support Systems

Deduced from expert systems research early Clinical Decision Support (CDS) were designed by its developers with rules that would allow computers to "think" like health professionals when confronted with a patient [32].

CDSs provide both expert clinicians and other persons with knowledge and person-specific information. This information is filtered and presented at appropriate times to improve health and health care [14].

To assist health professionals at the point of care is the main purpose of modern CDS [2]. Clinicians work with a Clinical Decision Support System (CDSS) which should help them to determine diagnosis, analysis or show alerts for specific patient data. This means such systems should not play the role as a physician but support them.

3.2 Types of Clinical Decision Support Systems

To support clinical decisions there are variant types of clinical decision support systems. Even systems like Medline[20] can assist health professionals in their decisions. Generally, first decision support systems have supported retrospective analyses of fincancial and administrative data[29]. Lately, complex data mining approaches for similar retrospective analyses of both administrative and clinical data have been proposed[4]. Despite using these retrospective approaches to develop guidelines or other systems to guide decision making at point of care, such retrospective analyses are not usually considered to be CDSS. To know this is important because suppliers often will provide their products including decision support capabilities, but their systems are not designed to assist clinicians at the point of care[2]. Because the interest of CDSSs increasing, vendors will integrate such types of CDS into their systems.

In obedience to a framework of Metzger and her colleagues[30][22], their CDSS using several dimensions which differ among themselves in the *timing* at the point it provide the service (before, during, or after the clinical decision is made). Another point the dimensions differ is how active or passive the system assits physicians and other health professionals (alerts on the fly or passively responds to the physician input or patient-specific information). Such systems also differ in wether the information provided is general or speciality-based. There are also noncommercials computerbased patient record

systems which incorporate CDSSs and vendors are beginning to integrate clinical decision support systems into their computer based patient records and physician order entry systems. An important categorization scheme for clinical decision support systems is, if they are knowledge-based clinical decision support systems or non-knowledge based systems that employ machine learning and/or other statistical pattern recognition CDSS[2]. The focus in the thesis is on the knowledge-based systems but other approaches will also be discussed.

3.2.1 Knowledge-based CDSS

Like above described, various knowledge-based CDSS which are used today originated out of past expert system's research, which were built to simulate human thinking [23][35]. First CDSS were developed for diagnostic decision support. Since the last twenty years the intent of these CDSSs was to assist health workers and not to simulate an expert's decision[2]. The system was expected to provide information for the user, rather than to come up with "the answer", as was the goal of earlier expert systems. To filter that information and find out errornous or useless information was the user's purpose. With such an approach the user can be active and interact with the system, rather than just be a passive recipient of the ouput. Such an interaction is important in setting appropriate expectations for the way the system will be used.
A knowledge-based clinical decision support system consists of three parts:

- A knowledge base which contains for example compiled clinical information on diagnoses, rules, associations of compiled data, drug interactions et cetera. A rule for drug interactions could be a IF...THEN rule, for example IF drug A is taken AND drug B is taken THEN show message to the user. In this case, the rule is designed to prevent that a patient will take two or more drugs which can interact, e.g. Brivudin (Zostex®) and 5-Flouropyrimidine and 5-Flourouracil (for therapy for breast carcinoma). Another example of knowledge bases might be a blood test[2]: IF a new order is placed for a particular blood test that tends to change very slowly, AND IF that blood test was ordered within the previous 48 hours, THEN alert the physician. In this case, the rule is designed to prevent duplicate test ordering.

- An inference enginge combines that knowledge with patient-specific information. It contains formulas for combining rules or associations in the knowledge base with actual patient data.

- Last but not least, there has to be a mechnism for the communication. The patient data need to get into the system and the system needs to bring the output to the user who will make the actual decision. In some systems the user needs to type in the data directly. In most cases a CDSS in inefrated into an electronic medical record system, the data are already in electronic form and come from the

computer-based patient record, where they were entered by health professionals, from laboratory or other hospital wards. One way to assist the pysician is to alert the information on the fly. Other methods are sending a message after the initial order was entered if the altert was triggered. Also possible is a system of email and wireless notification to send messages. Such an approach is already employed[17][34].

In a hospital or health center there are a lot of decisions where a system can assist health professionals. CDSSs have been developed for such situations. One example above describes a situation where a phycisian is prescribing two drugs which interact. Systems like this have been developed to provide a list of potential diagnoses to the users. Entered by the clinician or data already in the Electronic Medical Record (EMR), the system might start with the patient's signs and symptoms. The knowledge base of the decision support system contains information about diseases and their signs and symptoms. Now, the inference enginge maps these information to patient signs and symptomps and eventualls provide some information to the physician to assist his or her decision. It is important that a physician who knows the patient better than the computer system he or she uses, to eliminate some of the choices.

A system which provide support for medication orders is a good way to avoid medical errors, which are a major cause of death[16][10]. There are also CDSSs that are part of Computerized Physician Order Entry (CPOE) systems. The imput for the system might be the patient's laboratory test results for the blood level of a prescribed medication. The knowledge base might contain values for therapeutic and toxic blood concentrations of the medication and rules on what to do when a toxic level of medication is reached. If the medication level was too high, the ouput might be an alert to the physician[2].

3.2.2 Nonknowledge-based CDSS

Differently of knowledge-based clinical decision support systems, a form of artificial intelligence, called machine learning, is used by nonknowledge-based CDSSs in form of neural networks or genetic algorithms, id est, computers learn from past experience and/or find patterns in clinical data of an individual[41]. This two approaches are explained in the following sections.

Artificial Neural Networks

Artificial neural networks (ANN) simulate human thinking and learn from examples[41] and refer to the human brain. ANNs are spereated in two bigger fields[1]:

- Artificial neural networks which were modelled to understand easier the functionality of the human brain.

- Artificial neural networks to solve statistical problems in statistics, economics, technology and many other fields.

An ANN contains of several *neurons*. This neurons also called as *units* or *nodes*. Nodes are for taking information of other units or the environment and transfer modified information to other nodes or to the environment. There are three different kinds of neurons:

- Input-Units: Units, which get signals (pattern, stimuli) from the environment.

- Hidden-Units: Units, which are between Input- and Output-Units and contain internal representation of the environment.

- Output-Units: Units, which transfer signals (pattern, stimuli) to the environment
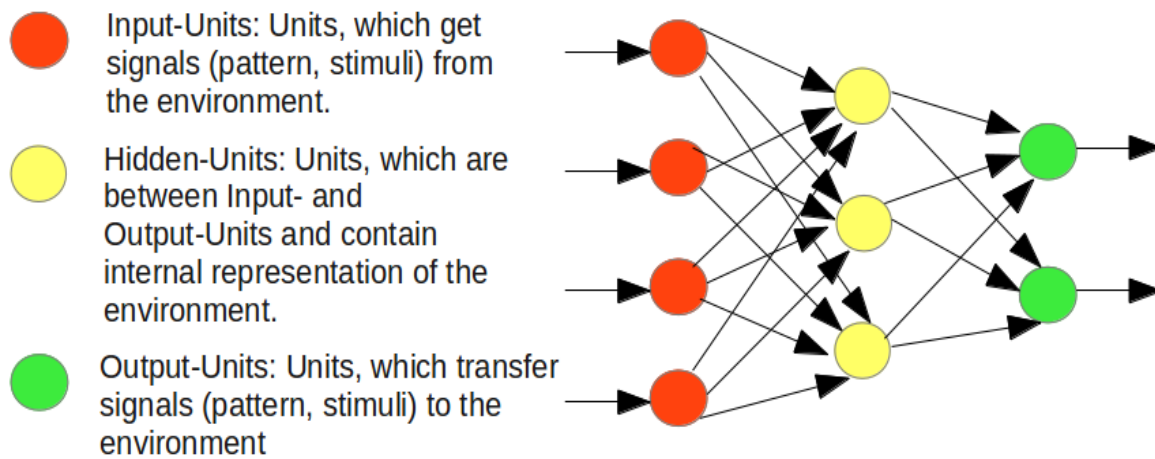
Figure 3.1: Schematic describtion of a neural network

Nodes on top of each other (for example the red output nodes) could be summarized as *layer*.

The connection between units is called an *edge*, the strength of a connection is enunciated as *connection weight*. The stronger the weight the bigger is the influence of a unit to another. There are three weights:

- *Positive weight* means this weight has an exitatory influence.

- *Negative weight* says the influence is inhibitory.

- A *weight of null* implies that a neuron has no influence to another one.

The knowledge of a network is saved in their weights. Changes in weight means the learning of a neural network. How a weight changes depends on the learning rule. The input which a neuron gets from another unit depends of two values, that are multiplied connected:

- Output (respectively activity level) of the sending unit

- Weight between two neurons

The stronger the activity level of the sending unit the highter is the weight between two units, the bigger is the influence (input) to the receiving unit. There is no influence

if one of the values euqals zero.

The whole input of a unit is called *netinput* which is defined through the *inputfunction*. The most wide spreaded function is a linear combination at which the netinput is composed additive of the other inputs that ae neuron gets from other neurons. Figured as formula:

$$input_{ij} = a_j \cdot w_{ij}$$
$$i = \text{he receiving unit and j the sending units}$$
$$a_j = \text{the activity level of the sending unit j}$$
$$w_{ij} = \text{the weight between j and i unit}$$
$$netinput_i = \sum_j input_{ij} = \sum_j a_j w_{ij}$$
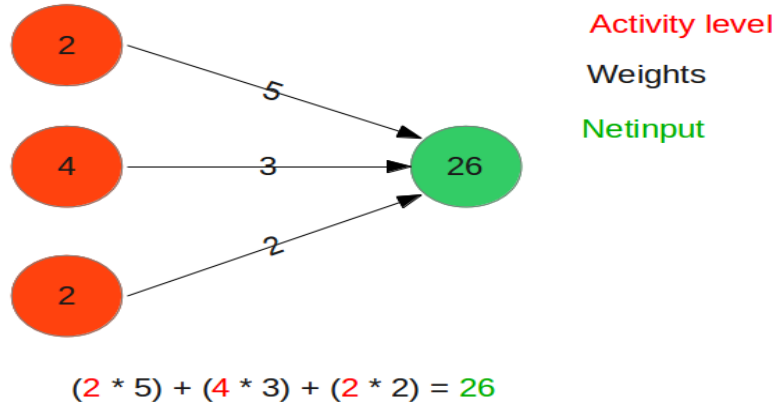
Figure 3.2: Calculation of netinput

This structure bears some similarities to the knowledge-based decision support systems, but rather than having a knowledge base derived from the medical literature or from an expert clinicians knowledge, the ANN analyzes the patterns in the patient data, to derive the associations between the patients signs and symptoms and a diagnosis. Many of the knowledge-based CDSSs cover a wide range of diseases. For instance, the input may be the signs and symptoms exhibited by a patient and the output may be the possible diseases the patient may have. Neural networks often focus on a more narrow range of signs and symptoms, for instance, those associated with a single disease, such as myocardial infarction[3].

If having a large amount of data, these systems can learn from examples when supplied with known results[12]. The system will study this information, make guesses for the

correct output, compare the guesses to the given results, find patterns that match the input to the correct output, and adjust the weights of the connections between the neurodes accordingly, in order, to produce the correct results. This iterative process is known as training the artificial network. In the example with myocardial infarction, for instance, the data including a variety of signs and symptoms from large numbers of patients who are known to either have or not have a myocardial infarction can be used to train the neural network. Once the network is trained, i.e., once the weighted associations of signs and symptoms withthe diagnosis are determined, the system can be used on new cases to determine if the patient has a myocardial infarction[2].

There are both advantages and disadvantages using ANNs. A big advantage is there is no need for direct inputs of experts and the need of writing IF...THEN... rules are dropped. Because of their dynamic nature ANNs can proccess incomplete data by inferring what the data should be and can improve every time they are used. Also not needed is a large database to make predictions about outcomes, but the more comprehensive the training data set is, the more accurate the ANN is likely to be[12]. A disadvantage is the time consuming proccess of training, because ANNs follow a statistical pattern recognition approach to derive their formulas for weighting and combining data. The results often not easily interpretable. Another problem is that the system could not explain why it uses certain data the way it does, which can make the reliability and accountability of these systems a concern[12].

There are studies which have shown, ANNs can predict which patients are at high risk for cancer such as oral cancer[26]. Predicting outcomes for surgery recovery or liver transplants are also possible with artificial neural networks as well as the analysis of waveform of electrocardiogramss (ECGs) and electroencephalograms (EEGs)[1].

Genetic Algorithms

In the 1940s, John Holland developed Generic Algorithms (GA). GAs simulate the process of natural evolution by Darwin which is about natural selection and surviving of the fittest[41]. To understand a genetic algorithm in computer science it is important to understand the organismic evolution. Just as species change to adapt to their environment, GAs *reproduce* themselves in various recombinations in an effort to find a new recombinant that is better adapted than its predecessors. In other words, without any domain-specific knowledge, components of random sets of solutions to a problem are evaluated, the best ones are kept and than recombined and mutated to form the next set of possible solutions to be evaluated, and this continues until the proper solution is discovered. The *fitness function* is used to determine which solutions are good and which one should be eliminated. GAs are similar to neural networks in that they derive their knowledge from patient data. Genetic algorithms have also been applied in health care, but there are fewer examples of this type of CDSSs than those based on neural networks. The following table shows the comparison of fundamental terms in biology and computer science.

Term	Biology	Computer science
Chromosome	Histone protein DNA	Cancidate solving
	Sets the characteristics of an individual in encoded form	
	mostly more chromosomes per individual	mostly only one chromosome per individual
Gene	Part of a chromosome	A character
	Basic unit of heredity which sets a part of the characteristics of an individual	
Allel	Peculiaritiy of a gene	Value of a character
	Per chromosome only one peculiarity of a gene	
Locus	Location of a gene	Position of a character
	In a chromosome at a location only one gene	
Phenotype	Composite of all characteristics of on organism	Implementation of a candidate solving
Genotype	Makeup of a cell, an organism or an individual	Encoding of a candidate solving
Generation	Population of a organism	Ppulation at a momentime
Reproduction	Generation of descendants of one or more organisms	Generation of a chromosome of one or more chromosomes
Fitness	Aptitude of an organism	Goodness of a candidate solving
	Affects the chances of survival and reproduction	

Table 3.1: Terms in biology and computer science by comparison

Genetic algorithms have also been applied in health care, but there are fewer examples of this type of CDSS than those based on neural networks. However, GAs have proved to be a helpful aid in the diagnosis of female urinary incontinence[18]. An genetic algorithm consists of following parts:

- coding regulation

- beginning population

- fitness function

- technique of sampling

- genetic operator

- parameter

- abort criteria

Research has shown that CDSSs based on pattern recognition and machine learning approaches may be more accurate than the average clinician in diagnosing the targeted diseases, many physicians are hesitant to use these CDSSs in their practice because the reasoning behind them is not transparent.

Most of the systems that are available today involve knowledge-based systems with rules, guidelines, or other compiled knowledge derived from the medical literature. The research on the effectiveness of CDSS has come largely from a few institutions where these systems were developed[2].

Example for GA

Nowadays there are a lot of areas where GAs are used. Exempli gratia for planes' wings. With GA the profile of wings gets optimized and tested with a computer simulation. Generally GAs helps solving NP-hard problems, for example the problem with a delivery service. The question is: "What is the best route for the delivery service? ".
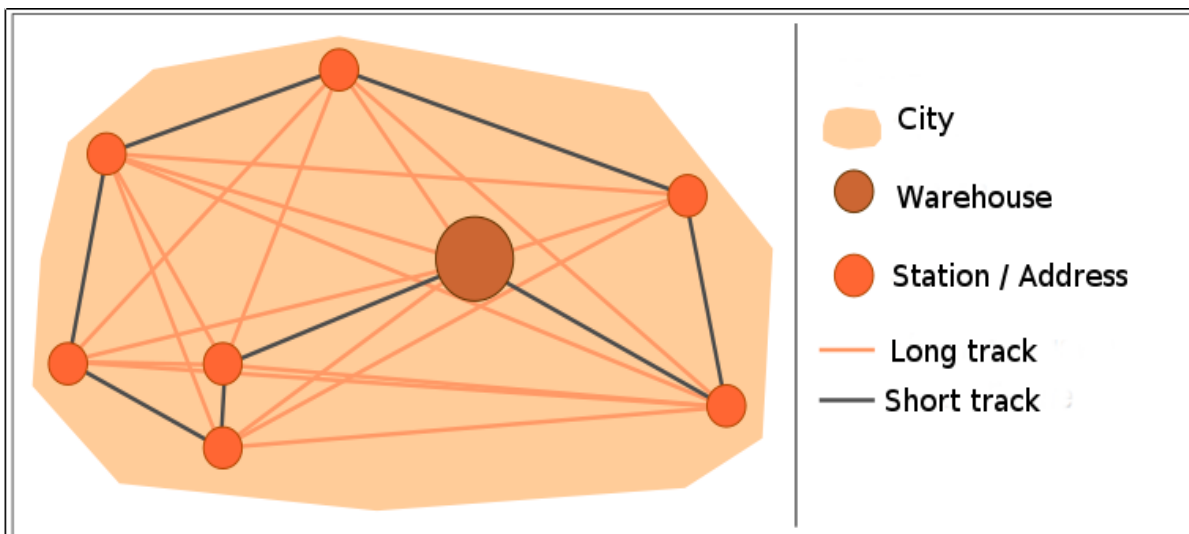
Figure 3.3: Schematic example for route planning

To get a good solution it is necessary to create a genetic algorithm which encodes the solution as n-tuple of figures, where n is the amount of enumerated stations. It is important that every station exists. The fitess function matches the tuples to the length of the way, multiplied with -1, so it is maximzed. To change a figure of a tuple is suitable for a mutation operator. But it is necessary that the tuple will be adapted in a second position, thereby the solution preserves its significance, because the figure, which is a station, should occur anywhere in the tuple. With *crossover* it is also important to take

care that crossed chromosomes represent valid solutions. For the case this is not, the crossover should be cancelled. The probability of the mutation and crossover can be defined through systematic testing. The chromosome with the best fitness at the end of the algorithm is the solution as the order for the stations.

4 Methods and Materials

4.1 Requirements analysis

The previous chapter described the environment for this work as a general hospital in Kampala and a health center in Mifumi. To know the workprocesses of the facilities it is important to see how health professionals work. Hence, why the author went to the facilities to get an overview of the environment for which the decision support system for drug interaction was designed. It was necessary for further steps to acquire knowledge about health system, infrastructure of the existing electronic information system and work flows in the hospitals and health centers. Also important was to get an impression of how the system is used by the hospital staff.

Therefore meeting trainings for the staff was important to see how health professionals work with eHMIS and integrate their work with it into their workflow. Because the elder generation of Uganda did not raise with computers in school they have problems to work with them and the work with an electronic information system is often slow.

Another point was the analysis of the environment to know how to design, develope and integrate the new module into the existing electronic health management information system. Because there is no documentation of eHMIS it was necessary to "play" with the system to know its workflows. The next sections describe the requirements of a decision support system in Uganda for eHMIS.

The functionalites of a Decision Support System (DSS) depends on both the issues it should solve and who will use it. In this thesis the focus is on a clinical decision support system.

1. **Add, edit, delete interaction**
   Every health professional with a specific knowledge of drugs, for example a pharmacist, must have the possibility to add new interactions to the system because of new drugs. To edit this interactions ins important because some drugs can change, for example the amount of an ingredient and that is why there is no interaction with other drugs anymore. Deleting is only necessary if a health facility stop using a drug.

2. **Show interaction**
   To assist a health professional in his or her work it is important that the system

informs him or her if there is an interaction. Possible methods, for example, are: 1) show a message in form of a dialog, 2) in form a writing the message directly in the window where the physician prescribes drugs and much more.

3. **On the fly**
   To not interrupt health workers in their work flow the messages for an interaction should be shown on the fly as soon as the health professional choose a drug for prescribing. Otherwise they need to re-check possible interaction after adding drugs for prescribing and than delete them, what is time consuming.

4. **Log**
   Logs are useful to create statistics, for example, how often an interaction was shown, which healt worker was the message shown and, if there are problems with the patient after taking the drugs, other physicians know which drugs the patient took and see which interaction with which problems could be.

As described above there are other funtionalities for different decision support systems, but these are only the most essential requirements for this thesis.

4.2 Technical environment

As in the introduction explained eHMIS is a browser-based system. eHMIS is implemented in PHP and JavaScript, its structure is Model, View, Controller (MVC) compliant. It contains eight main folders which are seperated into subfolders that correspond to the wards in the hospital and health center (actually implemented wards are: pharmacy, billing, eye clinic, laboratory, general clinic, outpatient department). The subfolders also contain PHP files for displaying, logic and other important files for the system.
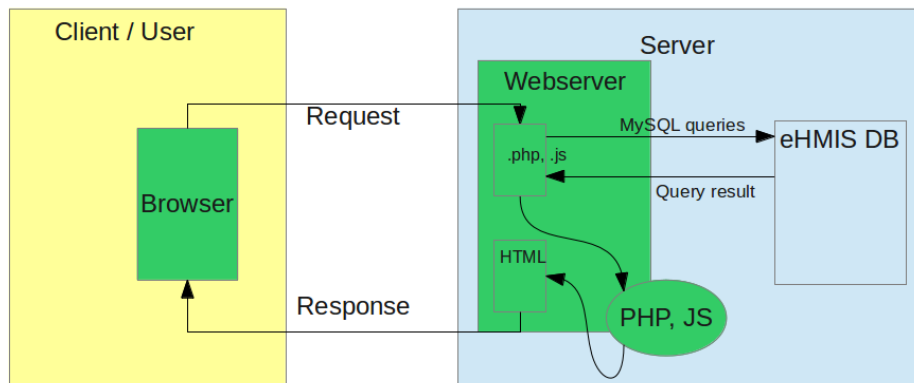
Figure 4.1: Client-Server-Model[43]

For starting eHMIS a user opens a Browser on his laptop or other workstation and types in the Uniform Resource Locator (URL) to get to the Login page (logon.php). Via

Hypertext Transfer Protocol (HTTP) the request is sent. "logon.php" will be identified as a PHP file in the web server and transferred by it to the Hypertext Preprocessor (PHP) interpreter. After execution of the PHP fragments in the file PHP than transfers a Hypertext Markup Language (HTML) file to the server. The HTML file now contains pure HTML code and will be sent back by the server[43]. At the backend a MySQL database is used for the management of persitent data. The connection is supported by MyODBC, the object database connectivity interface of MySQL database.

Figure 4.2: Structure of eHMIS

The electronical health information management system is MVC conform. Every part is seperated and the logic can be extracted as well as the controller to use for example

Java dialogs as view. A software architecture pattern is also useful for keeping track of a project.
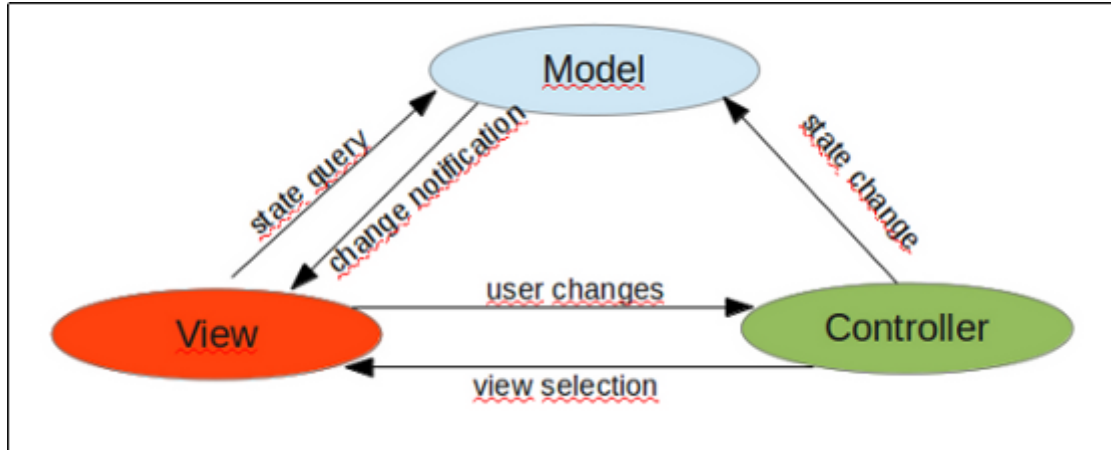
Figure 4.3: Scheme of MVC
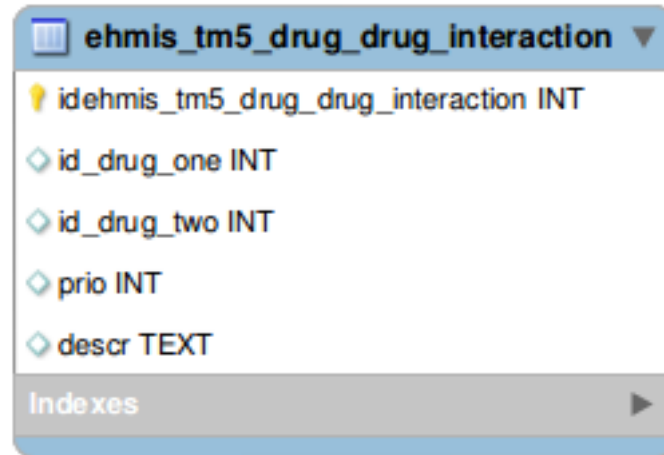
4.3 Implementation

To understand the implementation of the decision support system for drug interactions it is important to know the structure of eHMIS and its database.

4.3.1 Knowledge base

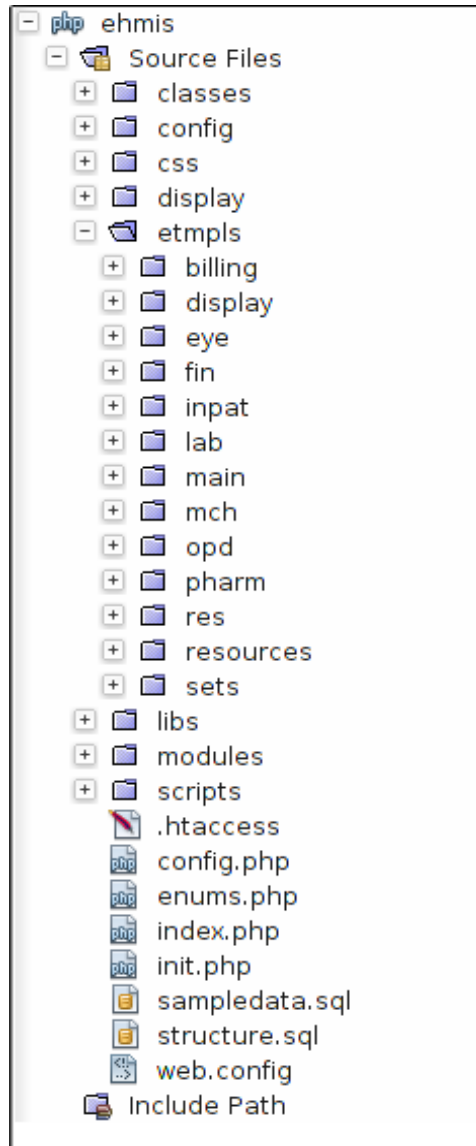Simon Ndira's eHMIS has a knowledge base in form of a MySQL database which contains all relevant information for an electronic medical system. For this thesis only some tables are needed, some new tables were created.
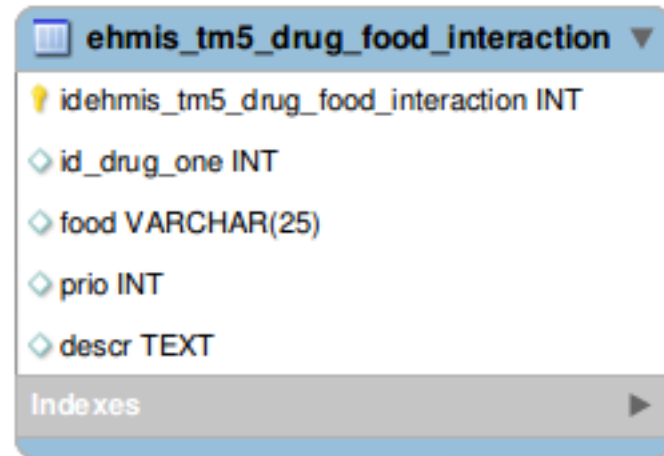
The original database consisted of 138 tables which are seperated into 12 different parts, for example patient data or data which are important for diagnosises like one for the International Statistical Classification of Diseases and Related Health Problems (ICD-10). For the new module 6 tables were created which contain the different interactions plus tracking for statistical matters. A priority is set for every interaction because of avoiding the so called over-alerting. Therefore a health professional can set which interactions with the setted priority he or she wants to see. Interactions are divided into three parts: red, orange and green (prio 1, 2, 3). For the tracking the first table (ehmis_tm5_drug_drug_interaction) consists of an id, id_drug_one, id_drug_two and a describtion (descr) of the interaction with a priority.

Figure 4.4: Table ehmis_tm5_drug_drug_interaction

Because of easier differentiation of interactions, different areas got sundry tables. The next table (ehmis_tm5_drug_food_interaction) contains the interactions of drugs with food, like alcohol or fruits. To show this interactions is necessary because a lot of people, also physicians, do not know these type of interactions. Columns of this table are: id, id_drug_one, food and a describtion (descr) as well as a priority.

Figure 4.5: Table ehmis_tm5_drug_food_interaction

For drug to condition interactions the module gets information about patient's condition from other tables already existed, but interactions are saved in an extra table (ehmis_tm5_drug_condition_interaction). It contains an id, an id_drug_one, condition_type (could be: pregnant, underweight, size of body and so on) and a describtion

(descr). It is connected to another table called ehmis_tm5_condition_type, which contains the describtions of conditions and last a priority.
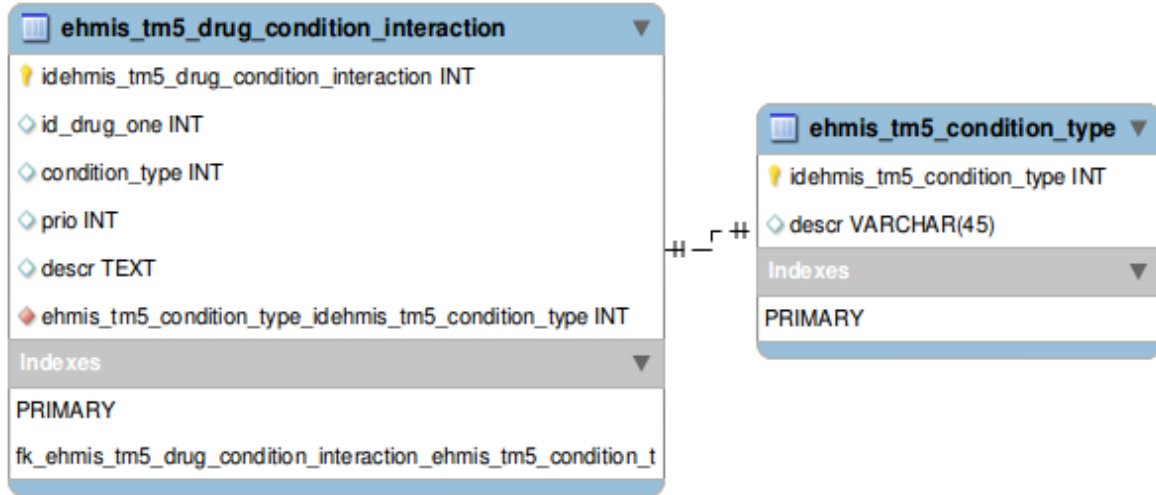
Figure 4.6: Table ehmis_tm5_drug_condition_interaction connected with ehmis_tm5_condition_type

Another a table for drug to disease interactions were created (ehmis_tm5_drug_disease_interaction). The U.S. Food and Drug Administration (FDA) [9] pools drug to disease interactions and drug to condition interactions. But in this thesis the areas are seperated for a better overview. The columns of the table are: id, id_drug_one, icd_code and a describtion (descr) as well as a priority.
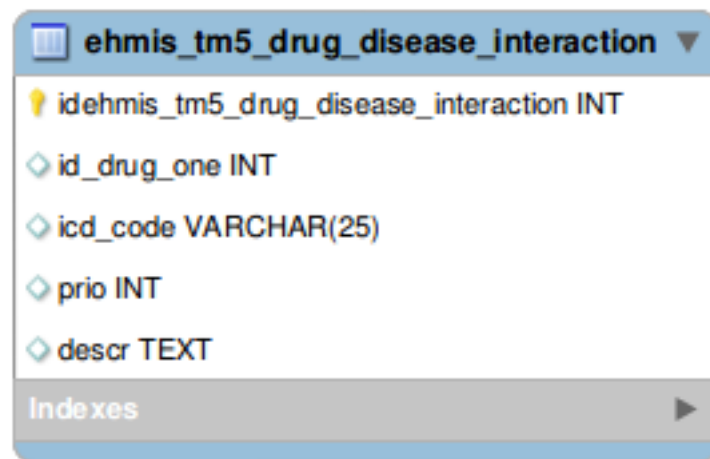
Figure 4.7: Table ehmis_tm5_drug_disease_interaction

Last but not least the tracking of interactions. Therefore 2 additional tables were created (ehmis_tm0_track_interactions, ehmis_tm0_interaction_type). The main table of

tracking is track_interactions. It is connected with the other tables and gets some information of a patient from the other tables already existing. Containing the type of interaction, an id of the interaction, patient's id, the case, a timestamp and priority as well as boolean and as foreign keys the ids of the other tables needed (information about the patient, for example the name, prename and id; data of the case, for example case_id; timestamp is the time when a health worker added a drug to the case; prio is the prioritey of the interaction; type could be drug to drug, drug to food, drug to condition and drug to disease with an ICD-10 code.) Most data of the interactions are from a free database called Drugbank[15]. It contains a lot of drugs with possible interactions and many other fields which are important for bioinformatics and cheminformatics. The database is supported by David Wishart, Departments of Computing Science & Biological Sciences, University of Alberta[40] and also by The Metabolomics Innovation Centre, a Genome Canada-funded core facility serving the scientific community and industry with world-class expertise and cutting-edge technologies in metabolomics[38].
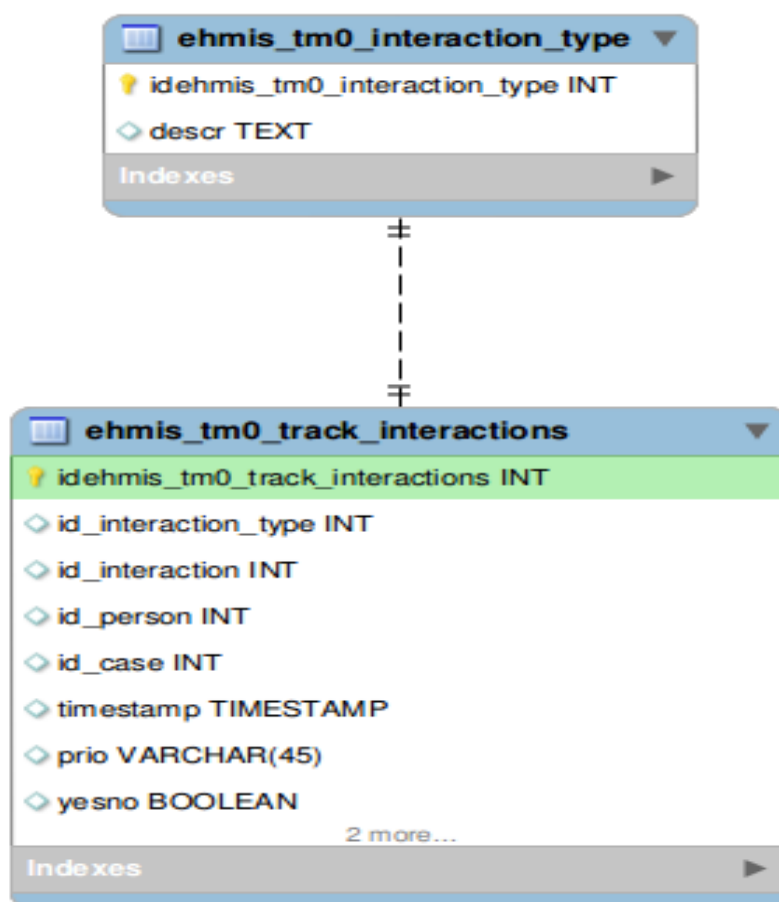
Figure 4.8: Tables for tracking interactions

4.3.2 Drug interactions

The idea was to implement a system for drug interactions for different areas, described in the following sections. As stated above the programming language is PHP and JavaScript. For a better overview, every interaction type is implemented in its own class. There is no parent class because they are too assorted among themselves.

At the end of this section screenshots will show how eHMIS and the new module look like.

Drug-to-drug interactions

The class *DrugDrugInteraction* has eleven variables and three functions: one for inserting a new drug-to-drug interaction into the knowledge base (*insertDrugDrugInteraction($vluList)*), a function called *getDrugDrugInteraction()* and a magical function, the so called *__construct()* function which get three variables: $id_drug_, $last_visit_, $prio_. Magical functions are predefined functions in PHP and will be executed if a specific action occurs.

DrugDrugInteraction

- id_drug
- id_patient
- last_visit
- gnrcs
- diff
- day
- prio
- pres
- ddi
- descri
- fldList

+ __construct()
+ insertDrugDrugInteraction($vluList)
+ getDrugDrugInteraction()
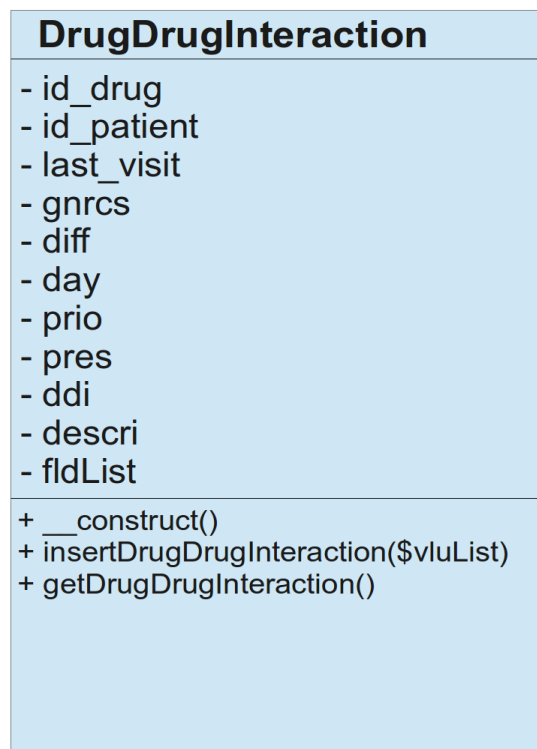
Figure 4.9: UML scheme of class DrugDrugInteraction

The function getDrugDrugInteraction() is only called if a patient already is taken at minimum one drug, otherwise there could not be any drug-to-drug interaction. In the

PHP file *tm0.medical.interaction.php* the function is assigned with Smarty, a template enginge for PHP. An assigned function is executed but without any return value.

Listing 4.1: Assign a function with smarty

```
$smarty->assign("DFI", $dfi);
```

After assigning the function it must be displayed. Therefore Smarty's function *void display(string template, string chache_id, string compile_id)* was used.

Listing 4.2: Display a function with smarty

```
$content = $smarty->display
        ('./main/medical/tm0.medical.interactions.tpl.html');
```
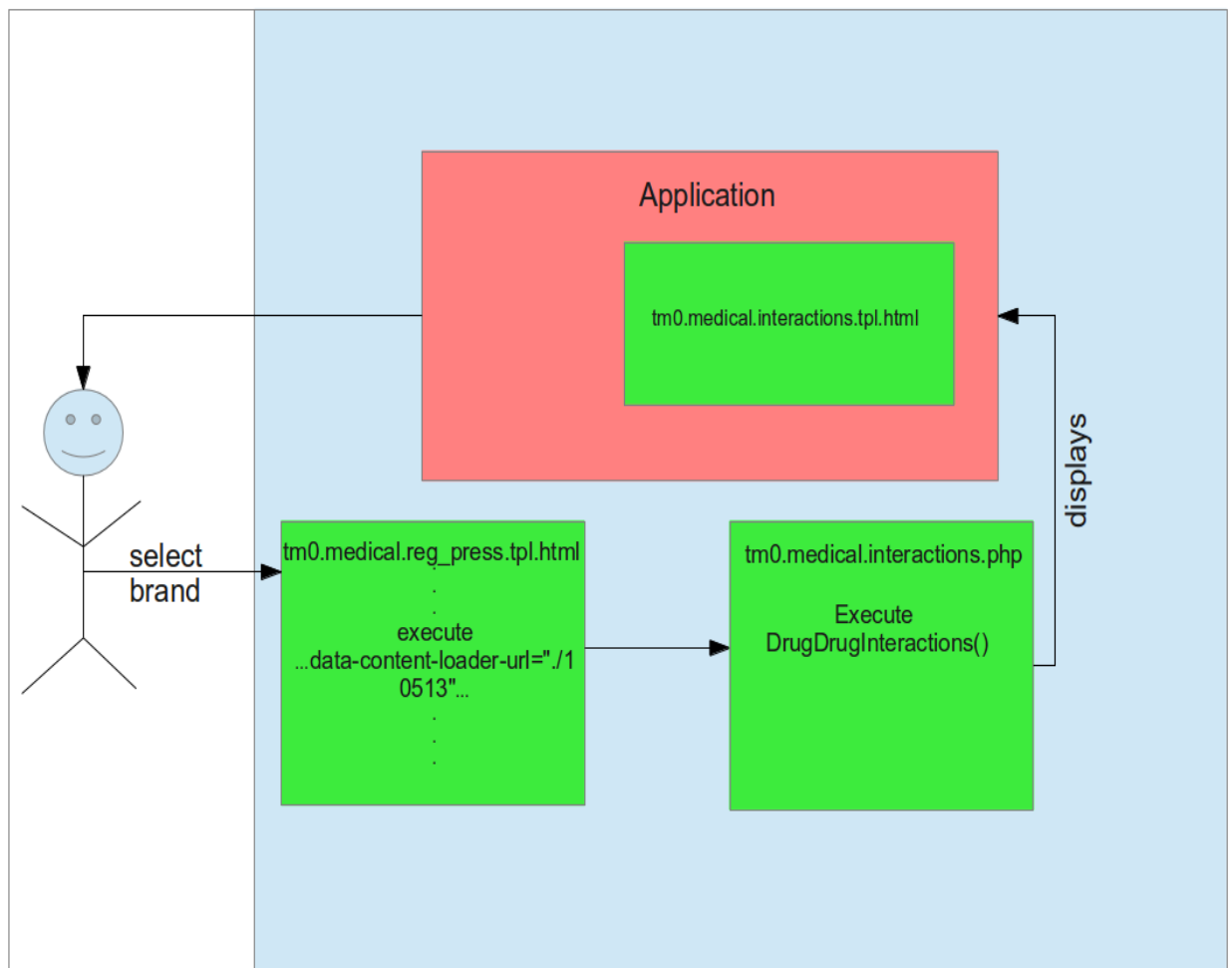

Figure 4.10: Workflow of calling a drug interaction

As a template serves the HTML file *tm0.medical.interactions.tpl.html*. This file only contains a HTML table with the interaction functions. To execute the file a health worker must select a drug (here with brand name). After typing in at minimum 3 letters of the name the system searches all generic names including this letters. Responsible for this is the function *tm0.medical.reg_press.tpl.html*. After selecting the correct brand tm0.medical.interactions.tpl.html is executed and the results of interactions are shown in the browser below the selected drug. For a drug-to-drug interaction only the drug's name could be enough but for drug-to-condition the exact brand is needed. This will be explained in section Drug-condition interaction.

Drug-to-food interactions

The first chapter describes drug-to-food interactions. This section explains the implementation of this module and shows the needed classes.

This type of interaction is more for patients than for health professionals. In Uganda, patients often get drugs without a patient information leaflet and the author's experience says a lot of Ugandans do not know about interactions between drugs and food. A health worker can print this information and give it to a patient.

DrugFoodInteraction

- id_drug
- last_visit
- dfi
- gnrcs
- diff
- day
- prio
- count
- descri
- fldList

+ __construct()
+ insertDrugFoodInteraction($vluList)
+ getDrugFoodInteraction()
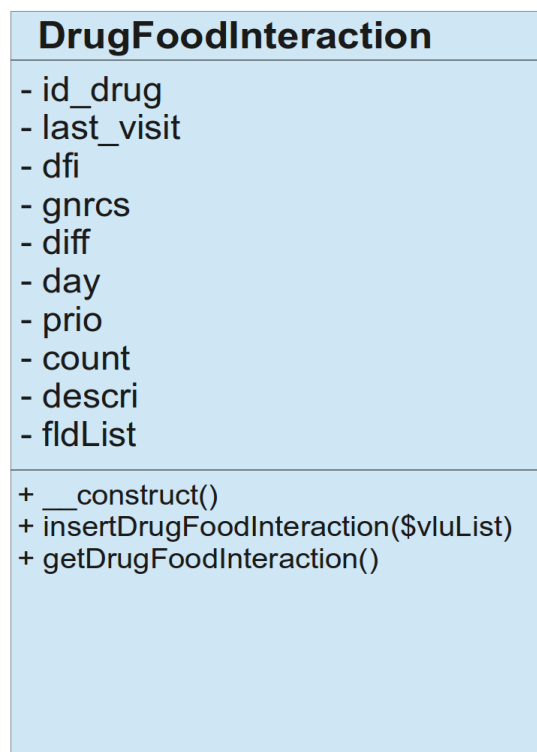
Figure 4.11: UML scheme of class DrugFoodInteraction

One of the functions, *insertDrugFoodInteraction($vluList)*, is responsible for adding a new drug-to-food interactions to the knowledge base. Therefore a name of the food is needed, for example *alcohol*, a drug with which the food interacts, a priority and a describtion (this values are saved in the $vluList). The drug id gehts the function from the system by selecting it in the data base. The variable *$lastVisit* is saved in a *$SESSION key*. $prio for the priority is a setup of a health worker saved in the data base.

The class *DrugFoodInteraction* has ten variables and also three functions. By calling the function *getDrugFoodInteraciton()* the system automatically calls the function *__construct()* and commits important variables: the drug's id, id of the last visit and the priority of which interactions a health worker wants to see.

Drug-to-disease interactions

This type of drug interaction also needs ten variables but five functions. Like the other modules it has a *__construct()* function, a function for inserting drug-to-disease interaction and than three *get-functions* for a interactionis itself, to get the actual diseases a patient has and if existing a chronical disease. This module is not completely implemented because the system do not has all impartant data available.

DrugDiseaseInteraction

- id_drug
- id_patient
- last_visit
- id_brand
- pres
- ddi
- diagnosis
- prio
- fldList

+ __construct()
+ insertDrugDiseaseInteraction()
+ getDrugDiseaseInteraction()
+ getActualDiseases()
+ getChronicalDiseases()
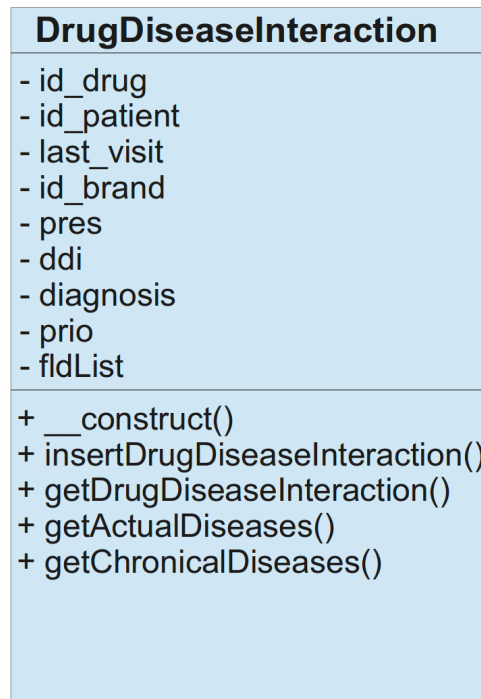
Figure 4.12: UML scheme of class DrugDiseaseInteraction

Drug-to-condition interactions

This modules is the most complex one. It consists of 25 variables and five functions. Described in the first chapter a drug-to-condition interaction could vary. There could be an interaction because of the weight or an existing pregnancy. Therefore all relevant patient data are needed, for example the weight, height, male or female.

DrugConditionInteraction

- id_drug
- id_patient
- id_brand
- age_from
- age_to
- condition_type
- indication
- toxicity
- halflife
- dosage_form
- person
- brnds
- wgt
- patAge
- pregnancy
- weight
- strength
- brand_name
- con_descr
- con_weight
- flds
- last_visit
- dfi
- prio
- fldList

+ __construct()
+ insertDrugConditionInteraction()
+ getDrugConditionInteraction()
+ setPatInfos()
+ setBrandInfos()
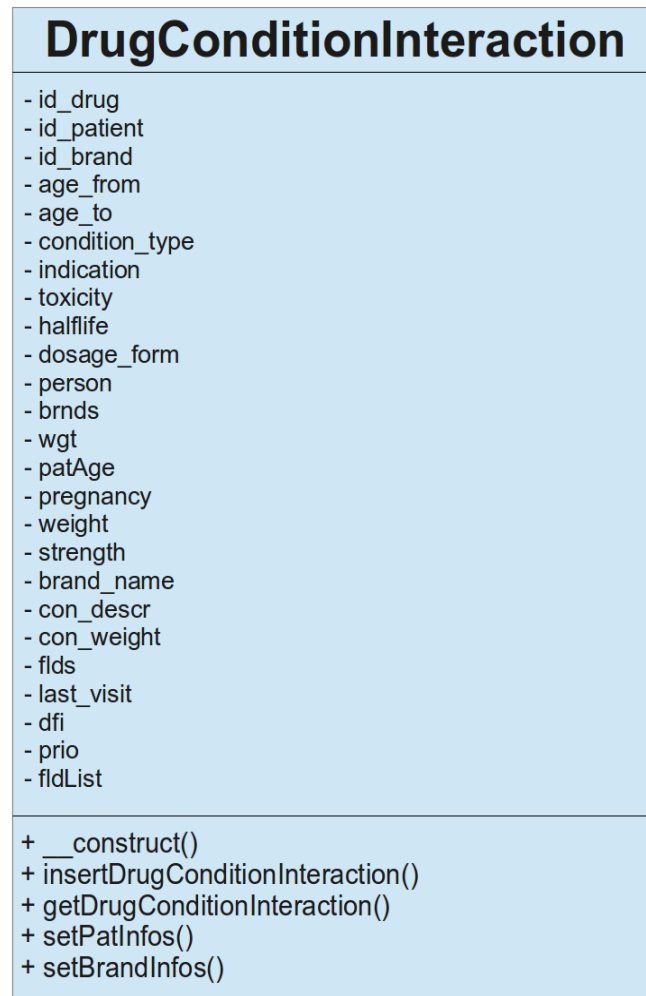
Figure 4.13: UML scheme of class DrugConditiongInteraction

Some drugs, for example Aspirin, could be too strong for a child or an underweight person, thats why it is necessary to konw which brand a physician want to prescribe. Paracetamol 600mg is too strong for small childs and a health professional may be do not know this. This module informs a health worker and says that it is too strong.

Add Prescription

Medicine

Search for Generic

IBUPROFEN

Select Brand

Ibumex 100mg/5ml BOTTLE, 0.00 ▸

Dosage

Dose

Frequency

Days

Start On   20 ▸   August ▸   2013 ▸

Diagnoses

☐ Plasmodium falciparum malaria

Cancel   Save

The following foods interact with IBUPROFEN:
- Alcohol: Never ever trink alc while taking ibuprofen.
There is an interaction between IBUPROFEN and
ASPIRIN:
Ibuprofen decreases the antiplatelet effects of
aspirin by blocking the active site of platelet
cyclooxygenase. The effect of other NSAIDs on
aspirin is not established.
There is an interaction between IBUPROFEN and
DIAZEPAM:
ibuprofen interagiert auch mit 10

41

Figure 4.14: Add prescribtion with showing interactions
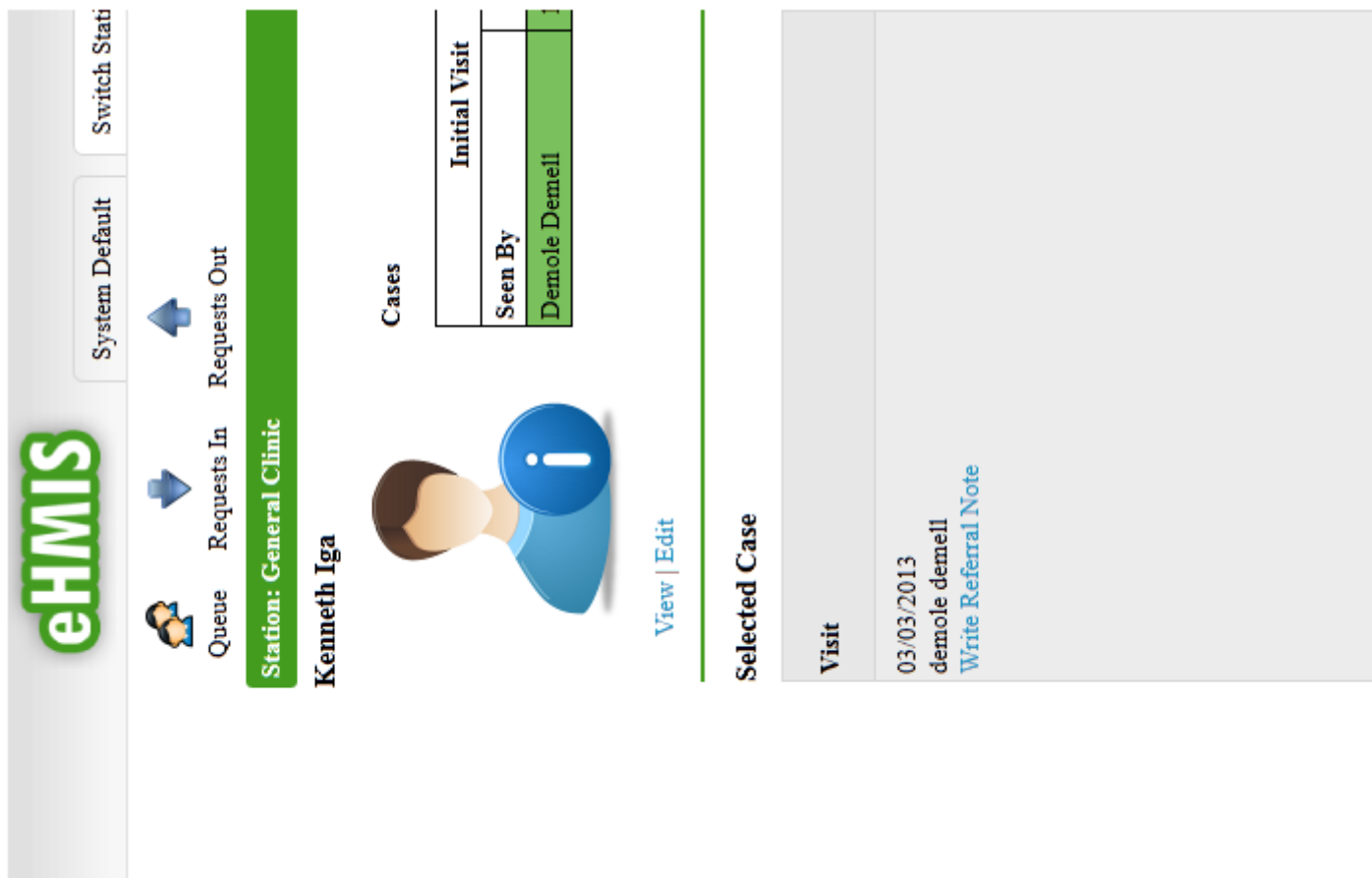
Figure 4.15: Main screen for diagnosises and cases 1

Date	#	Last Visit	Last Seen By
4/09/2012	2	03/03/2013	Demole Demell

Follow Up Summary

Notes - Add

This is the hardest event ever.
Edit | Delete

Diagnosis - Add

Angiodysplasia of colon
Maintained
Change Status | Delete

Calculus of bile duct with cholangitis
Maintained
Change Status | Delete

Caught, crushed, jammed, or pinched in or between objects
Maintained
Change Status | Delete

on

Figure 4.16: Main screen for diagnosises and cases 2

Welcome: Demole Demell | My Profile | Sign Out

Tickets

Inbound   Open:(0)   Closed:(0)
Outbound   Open:(0)   Closed:(0)

System Support

eHMIS is still under active development, and therefore any problems encountered during work, will be fixed in our next iteration.

- Management

Re-Queue

Current View Diagnosis, Prescription

Interactions
- Show

Prescription - Add

Aspirin 300mg TABLET
1 * 1 * 35
Maintain
Change Status
Change Brand | Undo Brand | Delete

Anti-snake Venom AMPOULE
2 * 1 * 35
Maintain
Change Status
Change Brand | Undo Brand | Delete

Heparin Sodium 5000 UI/ML AMPOULE
12 * 2 * 35
Maintain

Figure 4.17: Main screen for diagnosises and cases 3

5 Discussion

The previous chapters described how the CDSS was designed and implemented: starting with a describtion of the environment, analysis of the requirements of a clinical decision support system for drug interactions over other approaches to the implementation of the system. Now, this chapter discusses the thesis critically.

The present work has set a starting point for a clinical decision support system for drug interactions. The investigations should indicate that the use of a CDSS for drug interactions reduces medical problems because of wrong medication, but this is not part of this thesis.

5.1 Messages

5.1.1 Ignore message

Alerts are shown in the window where a health professional adds drugs. A problem could be that a physician works fast with the system and may be will overlook a message for an interaction or ignore it. May be a better solution is to open a new dialog automatically with all required information so a health worker needs to close that window first before he or she can work again with eHMIS.

5.1.2 Forget interaction

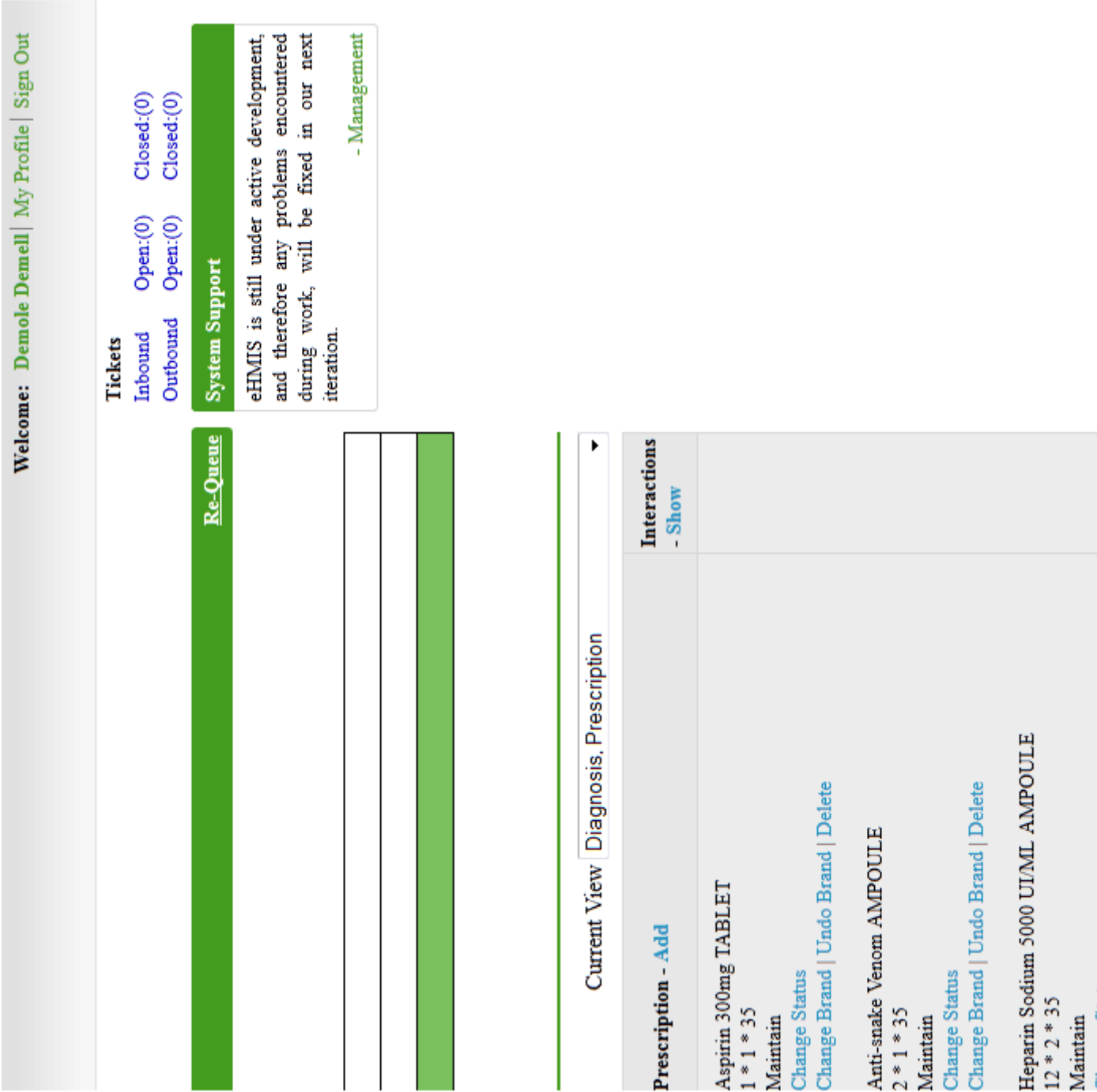After showing possible drug interactions there should also be a messaging system if a physician prescribed drugs notwithstanding they interact. Such a system could be another list in the window, where all diagnosises and cases are shown, and beside that list it could be another list with links which open dialogs containing the specific drug interactions.

5.2 Future Work

The system eHMIS is not complete. Some more modules are needed, for example for a child ward in a hospital. A very important part is the statistic. UBOS[39] uses District Health Information System 2 (DHIS2)[5] for managing routine reports in the health system. DHIS 2 is the simple, flexible and open-source information system with awesome visualization features including GIS, charts and pivot tables, completely web-based. To

integrate this system into eHMIS with either Statistical Data and Metadata Exchange (Health Domain) (SDMX-HD)[33] or Data Exchange Format (DXF)[7]. DHIS2 has the possibility to create automatically statistical reports. With such reports a country knows its health system better and can improve it step by step. eHMIS would be the first electronic medical system in Uganda connected with DHIS2.

In the last chapter, Appendix, there is a list of the Ministry of Health of Uganda, the so called *Essential Medicines and Health Supplies List for Uganda 2012*. This enumeration contains all essential drugs but not that one which are most used. To have a list with the most used drugs in Uganda could be an advantage because the Ministry of Health can save money when buying only drugs which are really needed.

6 Conclusion

In this Thesis, a clinical decision support system for drug interactions were designed and implemented. It was important to know the workflow of health professionals in the hospital as well as in the health center in Mifumi. Together with the eHMIS team the clinical decision support system for drug interactions were designed and implemented. To use free and/or cheap tools for the new module was also relevant to eHMIS, because health facilities in Uganda do not have a lot of money to spend. The basic requirements to the CDSS are:

- The system should be as cheap as possible or better completely for free,

- intuitive in handling,

- should have an overview for all drug interactions for a patient,

- an overview for all drug interactions,

- platform-independent and

- show critical alerts to health professionals.

On the basis of this requirements the CDSS were built with PHP and JavaScript. Because the knowledge base in form of a MySQL database already existed a knowledge-based approach were used with IF...THEN... rules like *IF patient is pregnant AND physician will prescribe a medication which is not good while pregnancy THEN show alert.* The module was integrated in the existing system with all of its workflows, so the usability is given and health professionals do not need to interrupt their workprocesses. The alerts are shown on the fly if a health worker will prescribe two drugs and they interact or if a patient's characteristics are bad with a specific medication, for example if the patient is a baby and thereby too young for a whole tablet of Paracetamol 500mg. Other features of the clinical decision support system are:

- Drug-to-drug interactions

- Drug-to-food interactions

- Drug-to-condition interactions

- Drug-to-disease interactions

There are a lot of free databases which contain drug interactions. The problem is most of them are only online accessable or they are too expensive for the health facilities. To access such a database online is hard because the internet conncection is very slow, a physician would need too long to know possible interactions. Another problem with online databases is they do not have other patient data for drug to condittion interactions. Also as you can see in the requirements, the alerts should be shown on the fly and with online databases this is not possible.

7 Appendix

7.1 Selected source code

Listing 7.1: Class of DrugDrugInteraction

```php
<?php

error_reporting(E_ALL);

class DrugDrugInteraction
{
    private $id_drug = 0;
    private $id_patient = -1;
    private $last_visit;
    private $pres = PRESC;
    private $ddi = DRUGTODRUG;
    private $gnrcs = GNRCS;
    private $diff = -1;
    private $day = -1;
    private $prio = 1;
    private $descri = "";
    private $fldList = "id_drug_one, id_drug_two, descr, prio";


    public function __construct($id_drug_, $last_visit_, $prio_)
    {
        $this->last_visit = $last_visit_;
        $this->id_drug = $id_drug_;
        $this->prio = $prio_;
        $this->id_patient = $_SESSION['client'];
    }

    public function insertDrugDrugInteraction($vluList)
    {
        $GLOBALS['ehmis']->doInsert($this->ddi, $this->fldList, $vluList);
    }
```

```php
public function getDrugDrugInteraction()
{
    $SQLMedDiff = "SELECT med, datediff(curdate(), startedOn)
                    as timediff,
            days FROM $this->pres WHERE visit = '$this->last_visit'";
    $takenMedis = $GLOBALS['db']->execute($SQLMedDiff);

  // print_r($takenMedis);
  // echo "<br>";

    $SQLInteraction2 = "select id_drug_one, id_drug_two, descr,
                        prio from $this->ddi where id_drug_two =
            '$this->id_drug' or id_drug_one = '$this->id_drug'";
    $interaction2 = $GLOBALS['db']->execute($SQLInteraction2);

    $SQL1 = "select name from $this->gnrcs where id =
                '$this->id_drug'";
    $mach = $GLOBALS['db']->execute($SQL1);

    foreach($interaction2 as $inter2)
    {
        if($inter2['prio'] >= $this->prio)
        {
            $SQL22 = "select name, id from $this->gnrcs
                    where id = " . $inter2['id_drug_one'];
            $mach22 = $GLOBALS['db']->execute($SQL22);

            if($this->id_drug == $inter2['id_drug_one'])
            {
                $SQL22 = "select name, id from $this->gnrcs
                    where id = " . $inter2['id_drug_two'];
                $mach22 = $GLOBALS['db']->execute($SQL22);

                //print_r($mach22);
            }

            foreach($takenMedis as $takenMedi)
            {
                $this->diff = $takenMedi['timediff'];
                $this->day = $takenMedi['days'];
```

```php
                    try
                    {
                        if ($this->diff < $this->day && $takenMedi['med']
                                == $mach22[0]['id'])
                        {
                            $this->descri = $this->descri . "There is an
                                interaction between " . $mach[0]['name'] .
                                    " and " .
                                $mach22[0]['name'] . ":<br>" .
                                $inter2['descr'] . "<br>";
                        }
                    }
                    catch (Exception $exc)
                    {
                        echo $exc->getTraceAsString();
                    }
                }//foreach($medis as $medi)
            }
            else
            {
                //must be deleted
                echo "There is an interaction, but
                        the priority is too low. <br>";
            }

        }//foreach($interaction2 as $inter2)
        //return $this->descri;
        return $this->descri;
    }

//check interaction of both sides

$SQLInteraction2 = "select id_drug_one, id_drug_two, descr from $ddi
where id_drug_two = '{$_POST['generic']}' or id_drug_one =
'{$_POST['generic']}'";

$interaction2 = $db->execute($SQLInteraction2);

$SQL1 = "select name from $gnrcs where id = '{$_POST['generic']}'";
$mach = $db->execute($SQL1);
```

```php
if(count($interaction2) == 0)
{
    //save new drug
}
else
{
    foreach($interaction2 as $inter2)
    {
        $SQL22 = "select name, id from $gnrcs where id = " .
                            $inter2['id_drug_one'];
        $mach22 = $db->execute($SQL22);

        if($_POST['generic'] == $inter2['id_drug_one'])
        {
            $SQL22 = "select name, id from $gnrcs where id = " .
                            $inter2['id_drug_two'];
            $mach22 = $db->execute($SQL22);
        }

        foreach($medis as $medi)
        {
            $diff = $medi['timediff'];
            $day = $medi['days'];

            //echo $medi['med'];
            //echo "<br>" . $mach22[0]['id'];

            if($diff<$day && $medi['med'] == $mach22[0]['id'])
            {
                echo "There is an interaction between " .
                        $mach[0]['name'] . " and " . $mach22[0]['name']
                        . "<br>";
            }
        }//foreach($medis as $medi)
    }//foreach($interaction2 as $inter2)
}//else (if(count($interaction2) == 0))
}
?>
```

Listing 7.2: HTML file tm.medical.interactions.tpl.html

```html
<table>
    <tr>
```

```
        <td>
            {$DFI}
            {$DRDI}
        </td>
    </tr>
</table>
```

Listing 7.3: PHP file tm0.medical.interactions.php

```php
<?php

$brds = BRANDS;

$brand = $_GET["brand_id"];
$fld = "gnrc";
$id_drug = $ehmis->fetchById($brds, id, $brand, $fld);
//$id_drug = $_SESSION['id_drug'];
$lastVisit = $_SESSION['lastVisit'];
$prio = 0;
$dose = 0;
$frequency = 0;
$days = 0;
$id_patient = -1;
$id_prof = -1;
$yesno = -1;


//if($brand != '')
//{

    $interactions_drdi = new DrugDrugInteraction ($id_drug,
     $lastVisit, $prio);
    $drdi = $interactions_drdi->getDrugDrugInteraction();

    $interactions_dfi = new DrugFoodInteraction($id_drug,
    $lastVisit, $prio);
    $dfi = $interactions_dfi->getDrugFoodInteraction();

    /*
    $interactions_dci = new DrugConditionInteraction($id_drug,
    $lastVisit, $prio, $brand);
    $dci = $interactions_dci->getDrugConditionInteraction();
//      echo $interactions->getDrugDrugInteraction();*/
```

```php
//}

$smarty->assign("DFI", $dfi);
$smarty->assign("DRDI", $drdi);
//$smarty->assign("DCI", $dci);
$content = $smarty->display
('./main/medical/tm0.medical.interactions.tpl.html');
exit();
?>
```

Listing 7.4: PHP file tm0.medical.serach_brands_ajax.php

```php
<?php

$gnrc = trim($_GET['id']);


$yes = InUse::YES;
$cond = "gnrc = '{$gnrc}' AND in_use = '{$yes}'";
$options = $ehmis->fetchAll(BRANDS, 'id', 'brand ASC', $cond);


$brands = array();
foreach ($options as $option) {
    $item = new Item($option['id']);

    ####### CHECK ITEM AVAILABILITY #############
    $stock = new Stock($item->id, $station->dispense_stn);
    $stock->fetchItemTotalQtyInStock();

    $brands[] = array('value' => $item->id, 'text' => "{$item->name}
    {$item->strength} {$item->form}",
                          'qty' => $stock->totalQtyInStock);
}

$smarty->assign("brands", $brands);

$smarty->display("./main/medical/tm0.medical.search_brands.tpl.html");
exit(0);
?>
```

7.2 Total deaths by cause

Place	Name	Amount	Percent
1	HIV/AIDS	65,762	17.70
2	Influenza & Pneumonia	38,919	10.48
3	Diarrhoeal diseases	37,645	10.13
4	Malaria	32,569	8.77
5	Stroke	15,762	4.24
6	Low Birth Weight	13,801	3.71
7	Coronary Heart Disease	13,569	3.65
8	Birth Trauma	12,869	3.46
9	Violence	11,373	3.06
10	Tuberculosis	9,867	2.66
11	Other Injuries	9,289	2.50
12	Road Traffic Accidents	8,192	2.21
13	Pertussis	6,475	1.74
14	Maternal Conditions	6,453	1.74
15	Diabetes Mellitus	5,967	1.61
16	Meningitis	5,702	1.53
17	Lung Disease	4,948	1.33
18	Poisonings	4,258	1.15
19	Congenital Anomalies	4,106	1.11
20	Measles	4,102	1.10
21	Malnutrition	3,605	0.97
22	Kidney Disease	3,463	0.93
23	Suicide	3,299	0.89
24	Trypanosomiasis	3,201	0.86
25	Hypertension	2,746	0.74
26	Schistosomiasis	2,614	0.70
27	Endocrine Disorders	2,480	0.67
28	Cervical Cancer	2,464	0.66
29	Fires	2,452	0.66
30	Drownings	2,447	0.66
31	Asthma	2,184	0.59
32	Epilepsy	2,133	0.57
33	Inflammatory/Heart	2,038	0.55
34	Lymphomas	1,725	0.46
35	War	1,656	0.45
36	Anaemia	1,627	0.44
37	Oesophagus Cancer	1,465	0.39

38	Syphilis	1,263	0.34
39	Prostate CancerS	1,249	0.34
40	Liver Disease	1,219	0.33
41	Liver Cancer	1,199	0.32
42	Breast Cancer	1,144	0.31
43	Stomach Cancer	1,120	0.30
44	Peptic Ulcer Disease	1,101	0.30
45	Falls	1,036	0.28
46	Vitamin A Deficiency	946	0.25
47	Alzheimers/Dementia	824	0.22
48	Other Neoplasms	662	0.18
49	Colon-Rectum Cancers	622	0.17
50	Oral Cancer	553	0.15

Table 7.1: Total deaths by cause[11]

7.3 Essential medicines

The following list contains essential medicines and health supplies for Uganda which are important for this thesis. The original list consists of much more drugs. It is written and corrected by the Ministry of Health, Republic of Uganda[13]. The first entry is the medicine's name, in the brackets is the dosage form, strength, level of use (level of facility), Vital (V), Essential (E), Necessary (N) (VEN) classification. Levels of facilities are:

- Blood bank (BB)

- National Referral Hospital(NRH)

- Regional laboratory (RL)

- Regional Referral Hospital (glslRRH)

- Hospital (H)

- Health centre 1 (community level) (HC I)

- HC II

- HC III

- HC IV

1. ***ANAESTHETICS***
   1.1 **General anaesthetics and oxygen**
   - Etomidate (Injection, 2mg/ml, RR, E)
   - Halothane (Liquid for inhalation, 100%, HC IV, V)
   - Oxygen (Medical gas, 99.8%, HC IV, V)

   1.2 **Local anaesthetics**
   - Bupivacaine (Injection, 0.5%, RR, V)
   - Lignocaine (Injection, 2%, HC II, V)

   1.3 **Preoperative and peri-operative medication**
   - Atropine (Injection, 1mg/ml, HC IV, V)
   - Diazepam (Injection, 5mg/ml, HC IV, V)

2. ***ANALGESICS, ANTIPYRETICS***
   2.1 **Non-opioids**
   - Acetylsalicylic acid (Tablet, 300mg, HC II, E)
   - Ibuprofen (Tablet, 25mg, HC III, E)
   - Paracetamol (Tablet 500mg, HC II, E)

   2.2 **Medicines used for gout**
   - Indomethacin (Capsule, 25mg, H, N)

   2.3 **Opioid analgesics**
   - Codeine (Tablet, 30mg, HC IV, E)
   - Morphine (Oral solution, 10mg/ml, HC III, E)
   - Pethidine (Injection, 50mg/ml, HC IV, V)

3. ***ANTI-ALLERGICS AND MEDICINES USED IN ANAPHYLAXIS***
   - Cetrizine (Tablet, 10mg, H, N)
   - Chlorphenamine maleate (Tablet, 4mg, HC II, E)
   - Epinephrine (Injection, 1mg/ml, HC II V)
   - Promethazine (Tablet, 25mg, HC II, E)

4. ***ANTIDOTES***
   4.1 **General antidotes**
   - Charcoal (Tablet, 250mg, HC II, E)
   - Flumazenil (Injection, 0.1mg/ml, H, V)

4.2 Specific antidotes

- Benztropine (Injection, 1mg/ml, H, E)
- Calcium gluconate (Injection, 10%, HC III, E)
- Naloxone (Injection, 400g/ml, NRH, E)

5. *ANTIEPILEPTICS AND ANTICONVULSANTS*

- Carbamazepine (Tablet, 200mg, HC III, V)
- Clonazepam (Tablet, 2mg, RRH, E)
- Valoproate (Tablet, 100mg, H, N)
- Diazepam (Rectal tube, 2mg/ml, HC II, V)

6. *ANTI-INFECTIVE MEDICINES*

6.1 Antihelmintics

i. *Intestinal antihelmintics*

- Albendazole (Tablet, 400mg, HC I, V)
- Mebendazole (Tablet, 500mg, HC II, E)
- Paracetamol (Tablet 500mg, HC II, E)

ii. *Antischistosomals*

- Praziquantel (Tablet, 600mg, HC IV, E)

6.2 Antibacterials

i. *Beta-Lactam medicines*

- Amoxicillin (Capsule, 500mg, HC II, V)
- Amoxicillin (Tablet, 250mg, HC II, V)
- Azithromycin (Tablet, 250mg, RRH, N)
- Benzylpenicillin (Powder for injection, 600mg, HC III, E)
- Cefixime (Tablet, 200mg, H, N)
- Ceftriaxone (Powder for injection, 1g, HC IV, V)
- Cloxacillin (Powder for injection, 500mg, HC IV, E)
- Vancomycin (Injection, 500mg, RRH, E)

ii. *Other antibacterial medicines*

- Chloramphenicol (Capsule, 250mg, HC III, V)
- Ciprofloxacin (Tablet, 250mg, HC III, V)
- Cotrimoxazole (Tablet, 125mg, HC II, V)

- Cotrimoxazole (Tablet, 480mg, HC II, V)
- Doxycycline (Tablet, 100mg, HC II, V)
- Erythromycin (Tablet (scored), 250mg, HC IV, N)
- Gentamicin (Injection, 40mg/ml, HC III, V)
- Metronidazole (Tablet, 200mg, HC II, V)
- Nalidixic acid (Tablet, 500mg, H, N)
- Nitrofurantoin (Tablet, 100mg, HC II, E)

  iii. ***Antileprosy medicines***
  - Prednisolone (Tablet, 20mg, HC III, E)
  - Rifampicin + dapsone (Tablet (blister), 600mg + 100mg, HC III, V)
  - Rifampicin + clofazimine + dapsone (Tablet (blister), 600mg + 300mg + 100mg, HC III, V)
  - Thalidomide (Tablet, 50mg, RRH, N)

6.3 Antifungal medicines

- Amphtericin B (Oral suspension, 100mg/ml, RRH, E)
- Clotrimazole (Pessary, 500mg, HC II, E)
- Griseofulvin (Tablet, 125mg, HC III, N)
- Miconazole (Pessary, 100mg, HC IV, N)
- Nystatin (Pessary, 100,000IU, HC III, E)

6.4 Antiprotozoal medicines

  i. ***Antiamoebic medicines***
  - Metronidazole (Tablet, 200mg, HC II], V)
  - Tinidazole (Tablet, 500mg, H, N)

  ii. ***Antimalarial medicines***
  - Artemether (Injection, 80mg/ml, HC III, E)
  - Artesunate (Injection, 60mg/ml, HC III, V)
  - Artesunate (Suppository, 50mg, HC I, V)
  - Artesunate + amodiaquine (Tablet, 50mg + 200mg, HC IV, E)
  - Chloroquine (Tablet, 155mg, HC IV, E)
  - Mefloquine (Tablet, 250mg, RRH, N)

  iii. ***Antitrichomoniasis medicines***
  - Tinidazole (Tablet, 500mg, RRH, NE)

iv. ***Medicines used in totoxoplasmosis***

- Clindamycin (Capsule, 150mg, H, E)
- Artesunate (Injection, 150mg/ml, H, E)

6.5 Antiviral medicines

- Aciclovir (Tablet, 200mg, HC IV, E)

7. *ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE MEDICINES*

- Betamethasone (Injection, 4mg/ml, HC IV, E)
- Prednisolone (Tablet, 5mlg, HC IV, E)

8. *IMMUNOLOGICALS*

8.1 Immunologicals, diagnostic medicienes

- Tuberculin purified protein derivative (Injection, 100IU/ml, HC IV, N)

8.2 Sera and immunoglobulins

- Anti-D immunoglobulin, human (Injection, 250g/ml, RRH, E)
- Antirabies immunoglobulin, human (Injection, 150IU/ml, H, V)
- Antiscorpionserum (Injection, mixture of *Androctonus*, *Leiurus* and *Buthus spp* in 10ml vial, RRH, N)
- Antitetanus immunoglobulin, human (Injection, 500IU, HC IV, V)

8.3 Vaccines

i. ***Vaccines for routine immunisation***

- Diphtheria-pertussis-tetanus (Suspension for injection, 25 LF *Diphtheria Toxoid*; 6 LF *Tetanus Toxoid*; 10,000 million *Borditella Pertussis* in 20-dose vial (10ml), HC II, V)
- Poliomyelitis vaccine, live attenuated (Oral suspension, 20-dose vial (2ml), HC II, V)

ii. ***Vaccines for specific groups of individuals***

- Anthrax vaccine (Injection, 0.125ml(anthrax antigens)/0.5ml dose, RRH, V)
- Hepatitis B vaccine (Intradermal injection, single-dose vial, HC IV, E)
- Human papilloma virus vaccine (type 16 + type 18 capsid protein)(Injection, 40g/ml + 40/ml, HC II, V)
- Meningococcal vaccine conjugate A+C (Injection, 0,5ml-vial, HC IV, E)

- Plague vaccine (Injection, Single-dose vial, H, N)
- Yellow fever vaccine, live (Injection, 1,000 LD50 units/0.5ml, H, N)

9. ***CARDIOVASCULAR MEDICINES***

   9.1 **Angianginal medicines**

   - Atenolol (Tablet, 100mg, H, V)
   - Glyceryl trinitrate (Tablet(sublingual), 500g, H, V)
   - Nifedipine (Tablet, 10mg, H, E)

   9.2 **Antidysrhythmic medicines**

   - Adenosine (Injection, 3mg/ml, RRH, E)
   - Propranolol (Tablet, 40mg, HC IV, E)

   9.3 **Antihypertensive medicines**

   - Captopril (Tablet, 100mg, H, E)
   - Enalapril (Tablet, 5mg, RRH, N)
   - Hydralazine (Tablet, 25mg, RRH, N)
   - Lisinopril (Tablet, 10mg, H, N)
   - Methyldopa (Tablet, 250mg, HC III, E)

   9.4 **Medicines used in heart failure**

   i. ***Cardiac glycosides***

   - Digoxin (Tablet, 62.5g, HC IV, E)
   - Digoxin (Injection, 250g/ml, H, N)

   ii. ***Medicines used in vascular shock***

   - Dopamine (Concentrate for IV inf, 40mg/ml, H, E)
   - Hydrocortisone sodium succinate (Powder for injection, 100mg, HC IV, E)

10. ***MUSCLE RELAXANTS AND CHOLINESTERASE INHIBITORS***

    - Cisatracurium (Injection, 2mg/ml, H, N)
    - Rocuronium (Injection, 10mg/ml, H, E)

11. ***OPHTHALMOLOGICAL PREPARATIONS***

    11.1 **Antiinfective medicines**

    - Chloramphenicol (Ophthalmic, 1%, HC II, N)
    - Chloramphenicol (Eye drops, 0.50%, HC II, N)

- Gentamicin (Drops for eye/ear, 0.30%, HC IV, N)
- Povidone (Eye drops, 5%, RRH, E)
- Tetracycline (Eye ointment, 1%, HC II, V)

11.2 Anti-inflammatory medicines

- Betamethasone (Eye drops, 0.10%, HC IV, N)
- Dexamethasone (Eye drops, 0.10%, RRH, E)
- Hydrocortisone (Eye ointment, 0.50%, HC IV, N)
- Prednisolone (Eye drops, 0.5.%, HC IV, E)
- Sodium chromoglycate (Eye drops, 2%, RRH, N)

11.3 Antifungal medicines

- Econazole (Eye drops, 2%, RRH, N)
- Natamycin (Ophthalmic suspension, 5%, RRH, N)

11.4 Antiviral medicines

- Aciclovir (Eye ointment, 3%, HC IV, E)
- Ganciclovir (Ophthalmic gel, 0.15%, RRH, E)

11.5 Local anaesthetics

- Bupivacaine (Injection, 0.5%, H, E)
- Hyaluronidase (Injection(powder for reconstitution), 1,500IU, RRH, E)

12. *PSYCHOTHERAPEUTIC MEDICINES*

- Amitriptyline (Tablet, 25mg, HC III, V)
- Benzhexol (Tablet, 2mg, HC II, V)
- Carbamazepine (Tablet, 200mg, HC IV, V)
- Chlorpromazine (Tablet, 25mg, HC II, E)
- Diazepam (Tablet, 5mg, HC II, V)
- Fluoxetine (Capsule, 20mg, H, V)
- Haloperidol (Tablet, mg, HC IV, E)
- Imipramine (Tablet, 25mg, HC IV, E)
- Promethazine (Tablet, 25mg, HC II, V)
- Trifouperazine (Tablet, 5mg, H, E)

13. *MEDICINES ACTING ON THE RESPIRATORY TRACT*

13.1 Antiashtmatic medicines

- Aminophylline (Tablet, 100mg, HC III, N)

- Beclomethasone (Aerosol inhalation, 50g/metered dose inhalation, HC IV, E)

- Prednisolone (Tablet, 5mg, HC IV, V)

- Salbutamol (Nebuliser solution, 2mg/ml, HC III, V)

13.2 Antitussive medicines

- Codeine (Tablet, 30mg, HC IV, E)

14. *VITAMINS AND MINERALS*

- Calcium lactate (Tablet, 300mg, HC III, N)

- Phytomenadione(vitamin K_1) (Injection, 1mg/ml, HC II, V)

- Retinol(vitamin A) (Capsule, 100,00IU, HC II, E)

- Thiamine (Tablet, 100mg, HC IV, E)

- Vitamin B compound(strong) ($B_5+B_6+B_2+B_1$) (Tablet, 20mg + 2mg + 2mg + 5mg, HC IV, N)

15. *EAR, NOSE AND OROPHARYNGEAL PREPARATIONS*

15.1 Ear preparations

- Betamethasone (Eye/ear drops, 0.10%, H, E)

- Clotrimazole (Solution, 1%, H, E)

- Gentamicin (Ear drops, 0.30%, H, V)

15.2 Nasal preparations

- Beclomethasone (Nasal spray(aqueous suspension), 50g/metered spray, H, N)

- Ephedrine (Nasal drops, 1%, H, E)

- Lignocaine + epinephrine (Nasal drops, 2% + 1:100,000, RRH, N)

15.3 Oropharyngeal preparations

- Lignocaine (Lozenge, 4%, HC IV, N)

- Miconazole (Oral gel, 24mg/ml(20mg/g), HC IV, N)

16. *ANTIRETROVIRAL MEDICINES*

16.1 Nucleoside/nucleotide reverse transcriptase inhibitors

- Abacavir (Oral solution, 20mg/ml, HC IV, E)

- Emtricitabine (Capsule, 200mg, HC IV, E)

- Lamivudine (Tablet, 150mg, Hc IV, N)

- Tenofovir (Tablet, 300mg, HC IV, N)

- Zidovudine (Oral solution, 10mg/ml, HC IV, V)

16.2 Non-nucleoside reverse transcriptase inhibitors

- Efavirenz (Tablet, 600mg, H, V)

- Nevirapine (Tablet, 200mg, H, V)

16.3 Dual fixed dose combinations

- Abacavir + lamivudine (Tablet, 60mg + 30mg, HC IV, E)

- Stavudine + lamivudine (Tablet, 6mg + 30mg, HC IV, V)

- Tenofovir + emtricitabine (Tablet, 300mg + 200mg, HC IV, N)

- Zidovudine + lamivudine (Tablet, 300mg + 150mg, HC IV, V)

16.4 Triple fixed dose combinations

- Stavudine + lamivudine + nevirapine (Dispersible tablet, 12mg + 60mg + 100mg, H, V)

- Tenofovir + emtricitabine + efavirenz (Tablet, 300mg + 200mg + 600mg, HC IV, N)

- Zidovudine + lamivudine + abacavir (Tablet, 300mg + 150mg + 300mg, RRH, N)

- Zidovudine + lamivudine + nevirapine (Tablet, 300mg + 150mg + 200mg, HC IV, V)

17. *NUTRITION*

- Formula 75, (Powder, 75kCal + 0.9g protein/100ml, H, V)

- Ready to use therapeutic-feeds (Paste, 30% full fat milk; 28%sugar; 15% vegetable oil; 15%peanut butter; 1.6% mineral vitamin mix, HC I, N)

18. *HORMONES, OTHER ENDOCRINE MEDICINES AND CONTRACEPTIVES*

18.1 Adrenal hormones and synthetic substitues

- Dexamethasone (Tablet, 0.5mg, H, N)

- Hydrocortisone (Powder for injection, 100mg, HC III, V)

- Prednisolone (Tablet, 5mg, HC IV, V)

18.2 Hormonal Contraceptives

- Ethinylestradio + levonorgestrel (Tablet 30g + 150g, HC II, E)

- Levonorgestrel (Tablet, 750g, HC I, V)

18.3 **Insulins and other antidiabetic medicines**

- Glibenclamide (Tablet, 5mg, HC IV, V)
- Insulin isophane (Injection, 100IU/ml, HC iV, V)
- Soluble insulin (Injection, 100IU/ml, HC IV, V)

18.4 **Thyroid hormones and antihyroid medicines**

- Carbimazole (Tablet, 5mg, H V)
- Levothyroxine (Tablet, 100g, H, V)

19. *DIURETICS*

- Bendrflumethiazide (Tablet, 5mg, HC III, E)
- Furosemide (Injection, 10mg/ml, HC IV, V)
- Spironolactone (Tablet, 50mg, H, N)

Acronyms

ANN Artificial neural networks. 22

BB Blood bank. 56

CDS Clinical Decision Support. 20

CDSS Clinical Decision Support System. 20

CPOE Computerized Physician Order Entry. 22

DHIS2 District Health Information System 2. 45

DSS Decision Support System. 29

DXF Data Exchange Format. 46

ECGs electrocardiogramss. 25

EEGs electroencephalograms. 25

eHMIS electronic Health Management Information System. 2, 10

EHR Electronic Health Record. 10

EMR Electronic Medical Record. 22

FDA U.S. Food and Drug Administration. 34

GA Generic Algorithms. 25

H Hospital. 56, 57, 59–65

HC I Health centre 1 (community level). 56, 59, 64, 65

HC II Health centre 2 (Enrolled Comprehensive Nurse). 18, 56–60, 62, 63

HC III Health centre 3 (Cinical Officer). 18, 56–59, 61, 63, 65

HC IV Health centre 4 (Medical Officer). 18, 56–65

HMIS Health Management Information System. 10, 18

HTML Hypertext Markup Language. 31

HTTP Hypertext Transfer Protocol. 31

ICD-10 International Statistical Classification of Diseases and Related Health Problems. 32

MoH Ministry of Health. 17

MVC Model, View, Controller. 30

NRH National Referral Hospitals. 17, 56

NSAID Non-steroidal anti-infflammatory drugs. 15

OPD Outpatient department. 10

PHP Private Hospitals. 17

PHP Hypertext Preprocessor. 31

PNFP Private Not For Profit. 17

RL Regional laboratory. 56

RRH Regional Referral Hospitals. 17, 58–64

SDMX-HD Statistical Data and Metadata Exchange (Health Domain). 46

UBOS Uganda Bureau Of Statistics. 17, 45

URL Uniform Resource Locator. 30

VEN Vital (V), Essential (E), Necessary (N). 56

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