Mobile Technology and Decision Support for the Administration of Antiretrovirals in Developing Countries

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A dissertation submitted to the University of Dublin, in partial fulfilment of the requirements for the degree of Master of Science in Health Informatics

2005
Declaration

I declare that the work described in this dissertation is, except where otherwise stated, entirely my own work, and has not been submitted as an exercise for a degree at this or any other university.

Signed:

Graham Woods
13/10/2005
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Acknowledgements

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Summary

As a result of the reduction in the price of patented Antiretrovirals (ARVs) and the increase in availability of generic ARVs, the potential exists to provide treatment to a greater number of people who are infected with HIV/AIDS. For a variety of reasons people living in sub-Saharan Africa do not have access to these treatments. One reason is that at present there is a lack of adequately trained clinicians to provide this treatment. If ARVs are not administered properly this will result in resistance or adverse reactions to the ARVs. Therefore training in the administering of ART is necessary and this issue must be addressed in order to reduce the likelihood of resistance to ARVs developing, due to their improper administration.

For clinical staff that are operating without the necessary training in the treatment and diagnosis of HIV/AIDS it is critical that they are provided with adequate support to help them recognize and diagnose symptoms of the virus. It is equally important that the Healthcare worker (HCW) is given support when deciding what course of action to take when administering care for a person living with HIV/AIDS.

This dissertation explores the potential use of a knowledge based application which uses clinical coding to aid the link between the Electronic Patient Record (EPR) and Clinical Practice Guidelines (CPGs). The application uses mobile technology to deliver support to HCWs who are administering ARVs in a resource deprived setting. Particular attention will be paid to the needs of HCWs operating in Uganda as result of contact being made with HIV/AIDS consultants from St James’ Hospital (SJH) Dublin who are currently based in Uganda. It is proposed that the codes will be recorded by the application, allowing the potential for a more efficient analysis of national or regional health data.

As part of the dissertation a small prototype was created which provides recommendations for the administration of ARVs. These recommendations are based on Uganda’s National Antiretroviral Treatment and Care Guidelines for Adults and Children. The prototype is hosted on a Personal

For the rest of this dissertation the term healthcare worker refers to a clinical person working at any level of the Ugandan health system who may or may not be medically qualified.
Digital Assistant (PDA) and the recommended regimen presented to the user reflects on the state of the patient, patient data stored in the EPR, and data input by the user.

For the purposes of this dissertation the codes proved a successful link when applied for this purpose although the extent to which they were tested was limited. By using the codes a standard method of naming a disease in the CPG can be used and as a result CPGs which are shared amongst institutions do not have to be altered in order to conform to a particular institutions naming scheme.
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Abbreviations
AIDS  Acquired Immunodeficiency Syndrome
API   Application Programming Interface
ART  Antiretroviral Therapy
ARV  Antiretroviral
ASTM American Society for Testing and Materials
BICS  Brigham Integrated Computing System
CLDC Connected Limited Device Configuration
CORBA Common Object Broker Request Architecture
CPG  Clinical Practice Guideline
CRHC Commonwealth Regional Health Committee
DALY Disease Adjusted Life Year
DIT  Dublin Institute of Technology
DNA  Deoxyribonucleic Acid
DOT Force Digital Opportunity Task Force
DRG  Diagnostic Related Group
ECA  Event-Condition-Action
EPR  Electronic Patient Record
FPG  Fasting Plasma Glucose
GLIF  Guideline Interchange Format
GP   General Practitioner
HAART Highly Active Antiretroviral Therapy
Hb   Haemoglobin
HCW Healthcare Workers
HEA  Higher Education Authority
HIV  Human Immunodeficiency Virus
HL7 Health Level 7
HR   Human Resources
HRH  Human Resources for Health
IAVI International AIDS Vaccine Initiative
ICD-10 International Classification of Diseases tenth version
ICD-10-AM ICD-10-Austrailian Modification
IDI  Infectious Diseases Institute
IE   Integration Engine
J2ME Java 2 Micro Edition
JNI  Java Native Interface
JVM  Java Virtual Machine
MARS Mobile Antiretroviral Support
MDC  Major Diagnostic Codes
MIDP Mobile Information Device Profile
MLMs Medical Logic Modules
MoH  Ministry of Health
MTCT Mother To Child Transmission
NGO  Non Government Organisation
NNRTI Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI  Nucleoside Reverse Transcriptase Inhibitor
OGTT Glucose Tolerance Test
OI   Opportunistic Infection
OS   Operating System
PDA  Personal Digital Assistant
<table>
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<td>Post Exposure Prophylaxis</td>
</tr>
<tr>
<td>PI</td>
<td>Protease Inhibitor</td>
</tr>
<tr>
<td>PLWA</td>
<td>People Living With AIDS</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic Acid</td>
</tr>
<tr>
<td>RPG</td>
<td>Random Plasma Glucose</td>
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<td>SD</td>
<td>Secure Digital</td>
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<td>UHS</td>
<td>Ugandan Health System</td>
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<td>UML</td>
<td>Unified Modelling Language</td>
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<tr>
<td>UN</td>
<td>United Nations</td>
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<td>VCT</td>
<td>Voluntary Counselling and Testing</td>
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<td>VLC</td>
<td>Viral Load Count</td>
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<tr>
<td>VM</td>
<td>Virtual Machine</td>
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<td>WfMS</td>
<td>Workflow Management Systems</td>
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<tr>
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<td>Wireless Fidelity</td>
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<td>XMI</td>
<td>Xml Metadata Interchange</td>
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1 Introduction

As a result of the reduction in price of patented ARVs and the increase in availability of generic ARVs, there exists the potential to provide treatment to a greater number of people who are infected with HIV/AIDS. For a variety of reasons people living in sub-Saharan Africa do not have access to these treatments. One reason is that at present there is a lack of adequately trained clinicians to provide this treatment. If ARVs are not administered properly this will result in resistance or adverse reactions to the ARVs. Therefore training for the administering treatment is necessary. This issue must be addressed in order to reduce the likelihood of resistance to ARVs developing, due to their improper administration.

For the clinical staff that are without the necessary training in the treatment and diagnosis of HIV/AIDS it is critical that they are provided with adequate support to help them recognize and diagnose symptoms of the virus. It is equally important that the HCW is given support when deciding what course of action to take when administering care for a person living with HIV/AIDS.

To date, African governments, Non-government Organisations (NGOs), international organisations and governments have invested large sums of money in developing structural resources for treating patients [1]. At the same time companies have also developed vaccines and treatments for diseases. However, many of these projects have failed to make an impact because of a lack of the necessary Human Resources for Health (HRH) [2]. In many cases, new laboratories and clinics lack the staff to operate them. For example in Mali, the government expanded the number of health posts to 533, but by January 2001 only 43 per cent were operating due to a lack of healthcare workers available to fill the vacancies [1]. In some countries the number of patients receiving Antiretroviral Therapy (ART) has had to be limited, not because the lack of ARVs but because of this shortage of HCWs [3].

There are a number of reasons for under staffing in African health systems. Traditionally there has always been an understaffing of HCWs in sub-Saharan Africa. In the 1980s the ratio of doctors per person was as high as 1 doctor for every 10,800 people and this poor ratio continued through the 1990s [4]. In rural areas and some urban areas, the ratio could even reach as high as one doctor for every 160,000. This problem has been exacerbated by the recent trend of African
Governments to cut back on the number of healthcare workers in an effort to reduce current expenditure on wages [1].

Another problem that has been increasing since the 1960s is the ‘Brain Drain’ of highly qualified workers from African countries. The total number of workers leaving a country is difficult to establish as many emigrants leave without making an official declaration of their departure [4]. It is therefore difficult for countries to plan for the future when unsure of the number of healthcare workers that it currently has, and what the current trends of emigration are.

In addition to understaffing and ‘brain drain’, there is an on going problem considering the health of HCWs. Between, 19 and 53 per cent of all public healthcare worker deaths arise from HIV/AIDS [1]. A related strain imposed on the health system arises from staff absenteeism when attending funerals. The Commonwealth Regional Health Community (CRHC) has reported that 14 per cent of all absenteeism is caused by people attending funerals of victims of AIDS [5]. Another 40 per cent of absenteeism is due to illnesses related to HIV/AIDS and the need to care for relatives of the suffering. The result is that the remaining healthcare workers, whose numbers are decreasing as a result of the fore-mentioned problems, are placed under greater pressure to treat the growing number of patients who are affected by HIV/AIDS [1][6].

All of these problems caused by HIV/AIDS have placed an even greater strain on health systems in Africa. By providing a HCW with access to information on the treatment of HIV/AIDS some of the strain caused by the disease could be alleviated by reducing the number of patients who fail firstline therapy. Also, by providing better ART a patient who has HIV/AIDS will be less infectious as their viral load will be lower.

1.1 Purpose of Study

This dissertation will explore the potential use of mobile technology to deliver decision support in administering ARVs to HCWs who are operating in a resource deprived setting. In order to provide support on treatment using ARVs there needs to be a link between the appropriate CPG and the patients’ clinical details. There will be an investigation into the use of a clinical coding scheme to aid the link between the EPR and CPGs. Figure 1 illustrates how this link will be provided.
As part of the dissertation a prototype known as Mobile AntiRetroviral Support (MARS) was created to provide HCWs with recommendations for the administration of ARVs. These recommendations will be based on Uganda’s National Antiretroviral Treatment and Care Guidelines for Adults and Children which were obtained from HIV/AIDS consultants from SJH who are currently based in Uganda. MARS is hosted on a PDA and the guidelines presented to the HCW reflect the state of the patient, based on patient data stored in the EPR, and data input by the user. The codes and the patient data will be recorded by the application, allowing the potential for a more efficient analysis of national or regional health data.

![Figure 1: Concept overview](image)

**1.2 Motivation**

The following points outline some of the reasons for choosing this particular area for research:

In 2004 three million people died of HIV/AIDS. It is also estimated that there was between 4.3 and 6.4 million cases of newly infected people. More than half of these cases were 15 to 24 years olds. This epidemic is placing a great strain on the health systems of sub-Saharan African countries [7].
There is currently a shortage of HCWs who are adequately trained in the provision of drugs that are used to treat HIV/AIDS in sub-Saharan African. Support needs to be given to these HCWs so that they administer these drugs correctly which will reduce the likelihood of resistance or adverse effects.

Guidelines for the treatment of HIV/AIDS are currently available in paper format in Uganda. However these guidelines have yet to be dispersed to the HCWs which is a common problem with text based guidelines. Another problem is that it is difficult to incorporate the guidelines into work practices when they are in this form. By converting the guidelines to electronic format it will be easier to disperse them and incorporate them into work practices.

In sub-Saharan Africa if a doctor is seen to be consulting a book it is assumed that they do not have the necessary experience. However if a doctor is seen to be looking up information electronically the perception is that they are well educated [8].

The number of people who are familiar with a PC is limited. Those that have access to a PC the availability of the internet is rare outside urban areas. In contrast to this the number of people who have a mobile phone is high (83.5% of the total telephone subscribers in 2001) [59]. Therefore mobile technology is a more acceptable method for presenting small amounts of clinical information electronically.

Additionally in rural parts of sub-Saharan African the constant supply of electricity is not guaranteed. By using a mobile device such as a PDA the effect of this shortcoming is nullified as such a device has a long battery life. It is also possible for these devices to charged using solar panels [18].

In the vast majority of clinics patient data is recorded on paper. Therefore it is difficult to evaluate statistics regarding patients who are infected with HIV/AIDS. It is important to be able to evaluate these statistics as the greater part of research on the disease has been conducted on western patients. Additionally it is essential to record what drugs are being taken by patients for accountability reasons.
1.3 Methodology

Initially informal interviews were held with specialists in HIV/AIDS from SJH to gain an understanding of the disease. Also the guidelines for delivering ART in Uganda were supplied by the specialists and these were reviewed. In order to assess the data that is collected on patients infected with HIV/AIDS and to gain domain knowledge a trip to Uganda was undertaken. Clinics in session in the Infectious Diseases Institute (IDI), Mulago Hospital, Kampala, were attended. Interviews were held with the CEO of the Satellife project which provided an insight into the structure of the Ugandan Health System (UHS) and how patient data is currently recorded.

A semi-structured interview and email correspondence was conducted with a member of the casemix department in SJH. From these communications and a review of the ICD-AM-10 literature an understanding of how HIV/AIDS is clinically coded was developed.

Another topic reviewed as part of this dissertation was clinical guidelines and the various methods of representing them electronically. This review consisted of an examination of papers from journals. An interview was also held with a member of staff in Tallaght Hospital to gain an insight into a decision support system called TRiPS which is currently in operation there.

Numerous J2ME books were read and online tutorials completed in order to develop the required programming skills. Two versions of MARS were created as part of this dissertation – MARS 1.0 and MARS 2.0. The first version consisted of creating an electronic version of the paper guidelines. After an evaluation (Section 7.1) of this version by African doctors who were being trained in the provision of ART, it was identified there was little difference in the performance of the electronic guidelines when compared with the paper based version of the guidelines. The second version, MARS 2.0 attempted to improve on the first version by encapsulating the CPGs by using an electronic guideline architecture, therefore reducing the need for a HCW to search for the appropriate information. A limited evaluation of this version was then performed by a range of HCWs for accuracy, usability and efficiency. Additionally articles from the web and computer magazines were assessed to identify the different types of PDA that currently exist.

From this point forward, any reference made to MARS will refer to the second version unless stated otherwise.
1.4 Outline of Dissertation

The following is an overview of the layout of this dissertation.

Chapter 1: introduces the scope of the dissertation. Reasons for choosing the domain of HIV/AIDS are identified. There is also a description of how the information contained in the dissertation was retrieved. Finally a layout to the dissertation is provided.

Chapter 2: The impact that the disease has on the world is identified and comparisons between the effect that virus has on the developed world and the developing world are outlined. Additionally, the gap in treatment methods which exist between the developed world and the developing world is highlighted. This leads to a description of the human resources (HR) crisis that the health systems in sub-Saharan Africa are currently experiencing. The effect that HIV/AIDS has on this crisis is also outlined. Finally an account of the impact that HIV/AIDS is having in Uganda is provided which also includes a summation of the UHS.

Chapter 3: This chapter provides a concise overview of the virus’s life cycle. This is followed by an outline of the different stages that a patient infected with HIV/AIDS goes through. The chapter also informs the reader of the different classes of ARVs which exist. Finally the recommendations for combining these classes of ARVs in Uganda are provided. Coupled with chapter 2 this chapter gives the reader a comprehensive understanding of the domain.

Chapter 4: This chapter provides an introduction to CPGs which is followed by a review of some of the different methods available for representing CPGs electronically. The reader is then presented with a summary of the proposed method for linking CPGs with patient data – clinical coding. This includes an overview of how HIV/AIDS is coded using the International Classification of Diseases - 9th Version (ICD-9) and ICD-10-Australian Modification (ICD-10-AM) coding schemes. In addition, clinical data required to create a CPG for treating HIV/AIDS that was extracted from the Ugandan guidelines is presented.

Chapter 5: This chapter provides an introduction to PDAs which includes a comparison between Pocket PCs and Palm PDAs. Accounts of projects where PDAs have been deployed in resource starved health systems are also given. Design issues to be considered when creating an application for a mobile device are also outlined. Finally important features of the programming language J2ME which is tailored for mobile devices are described.
Chapter 6: This chapter looks to build on previous discussions in order to create the MARS application. This is achieved by identifying the user requirements and a method for representing the guidelines electronically. Once the user requirements and guideline architecture is established a description of how they are applied to the MARS application is given. In addition, user interaction and some limitations to the application’s creation are explored.

Chapter 7: This chapter describes evaluations of MARS 1.0 and MARS 2.0. Results of the evaluations are presented along with any feedback obtained.

Chapter 8: This chapter outlines further enhancements that could be made to the application. It also presents any conclusions that were made.


2 Domain Description

This chapter provides a ‘state of the art’ of HIV/AIDS. The impact that the disease has on the world is identified and comparisons between the effect that virus has on the developed world and the developing world are outlined. Additionally, the gap in treatment methods which exist in the developed world and the developing world is highlighted. This leads to a description of the HR crisis that the health systems in sub-Saharan Africa are currently experiencing. The effect that HIV/AIDS has on this crisis is also outlined. Finally an account of the impact that HIV/AIDS is having in Uganda is provided which also includes a summation of the UHS.

2.1 Impact of HIV/AIDS on the World

Globally, the average life expectancy has risen by 20 years in the last half century [11]. Currently the developed world experiences an average life expectancy of 78 years of age. However these statistics tend to reflect on the health of the developing world. In parts of sub-Saharan Africa the average life expectancy has been in decline since 1990 and it is now at a similar level to region’s life expectancy of 30 years ago. According the 2003 World Health Report life expectancy would be over six times greater in these areas if it were not for HIV/AIDS [11].

HIV/AIDS claimed over 3 million lives in 2004 and 20 million people have died in total as a result of the disease. According to the UNAIDS/WHO in December of 2004 there were between 35.9 and 44.3 million people living with AIDS (PLWA) in the world. In addition to this the UNAIDS/WHO report estimates that in 2004 the number of new cases of HIV ranges from 4.3 to 6.4 million and more than half of these cases were people aged between 15 and 24 [6]. The International AIDS Vaccine Initiative (IAVI) predicts that a vaccine will be developed within the next decade [9]. Taking this into account along with the current infection rate between 43 and 64 million new cases may occur in the next 10 years.

Of the 3 million people who died because of the virus in 2004, approximately 90% of these deaths occurred in sub-Saharan Africa. Every hour it is estimated that 6,000 people die in this region as a result of the disease and one in six of these deaths relates to a child [6][10]. However on their own, mortality statistics do not portray the impact that HIV/AIDS has on the world as they fail to take into account the burden that the disease causes while the patient is alive. Disease Adjusted Life Years (DALYs) attempt to address this shortcoming by combining the years of life
lost through premature death and the years lived with disability. According to the WHO “One DALY can be thought of as one lost year of “healthy” life. The measured disease burden is the gap between a population’s health status and that of a normative global reference population with high life expectancy lived in full health [11].

Figure 2 and Figure 3 highlight the fact that in 2002, HIV/AIDS causes the greatest burden in world. Another important point to note about these figures is the age range (15 to 59), which accounts for the majority of the population workforce. With the majority of the PLWA residing sub-Saharan Africa this region is carrying most of the burden. The problem is further compounded as HIV/AIDS causes the spread of other diseases of heavy burden, notably tuberculosis.
### Mortality – adults aged 15-59

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<thead>
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<tr>
<td>1</td>
<td>HIV/AIDS</td>
<td>2279</td>
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<tr>
<td>2</td>
<td>Ischemic heart disease</td>
<td>1332</td>
</tr>
<tr>
<td>3</td>
<td>Tuberculosis</td>
<td>1096</td>
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<td>4</td>
<td>Road traffic injuries</td>
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<td>5</td>
<td>Cerebrovascular disease</td>
<td>783</td>
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<td>6</td>
<td>Self-inflicted injuries</td>
<td>672</td>
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<td>7</td>
<td>Violence</td>
<td>473</td>
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<tr>
<td>8</td>
<td>Cirrhosis of the liver</td>
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</tr>
<tr>
<td>9</td>
<td>Lower respiratory infections</td>
<td>352</td>
</tr>
<tr>
<td>10</td>
<td>Chronic obstructive pulmonary disease</td>
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### Mortality – adults aged 60+

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<td>2</td>
<td>Cerebrovascular disease</td>
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<td>3</td>
<td>Chronic obstructive pulmonary disease</td>
<td>2399</td>
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<tr>
<td>4</td>
<td>Lower respiratory infections</td>
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</tr>
<tr>
<td>5</td>
<td>Trachea, bronchus, lung cancers</td>
<td>928</td>
</tr>
<tr>
<td>6</td>
<td>Diabetes mellitus</td>
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<td>Hypertensive heart disease</td>
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<td>8</td>
<td>Stomach cancer</td>
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<td>9</td>
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<td>10</td>
<td>Colon and rectum cancers</td>
<td>471</td>
</tr>
</tbody>
</table>

### Disease burden – adults aged 15-59

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>DALYs (000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HIV/AIDS</td>
<td>68 661</td>
</tr>
<tr>
<td>2</td>
<td>Unipolar depressive disorders</td>
<td>57 843</td>
</tr>
<tr>
<td>3</td>
<td>Tuberculosis</td>
<td>28 381</td>
</tr>
<tr>
<td>4</td>
<td>Road traffic injuries</td>
<td>27 204</td>
</tr>
<tr>
<td>5</td>
<td>Ischemic heart disease</td>
<td>26 155</td>
</tr>
<tr>
<td>6</td>
<td>Alcohol use disorders</td>
<td>19 567</td>
</tr>
<tr>
<td>7</td>
<td>Hearing loss, adult onset</td>
<td>19 496</td>
</tr>
<tr>
<td>8</td>
<td>Violence</td>
<td>18 962</td>
</tr>
<tr>
<td>9</td>
<td>Cerebrovascular disease</td>
<td>18 749</td>
</tr>
<tr>
<td>10</td>
<td>Self-inflicted injuries</td>
<td>18 572</td>
</tr>
</tbody>
</table>

### Disease burden – adults aged 60+

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>DALYs (000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ischaemic heart disease</td>
<td>31 481</td>
</tr>
<tr>
<td>2</td>
<td>Cerebrovascular disease</td>
<td>29 595</td>
</tr>
<tr>
<td>3</td>
<td>Chronic obstructive pulmonary disease</td>
<td>14 380</td>
</tr>
<tr>
<td>4</td>
<td>Alzheimer and other dementias</td>
<td>8 503</td>
</tr>
<tr>
<td>5</td>
<td>Cataracts</td>
<td>7 381</td>
</tr>
<tr>
<td>6</td>
<td>Lower respiratory infections</td>
<td>6 597</td>
</tr>
<tr>
<td>7</td>
<td>Hearing loss, adult onset</td>
<td>6 545</td>
</tr>
<tr>
<td>8</td>
<td>Trachea, bronchus, lung cancers</td>
<td>5 052</td>
</tr>
<tr>
<td>9</td>
<td>Diabetes mellitus</td>
<td>5 882</td>
</tr>
<tr>
<td>10</td>
<td>Vision disorders, age-related and other</td>
<td>4 766</td>
</tr>
</tbody>
</table>

---

**Figure 2:** Leading causes of Mortality and Disease burden, 2002, [11]

**Figure 3:** Probability of Death between 15-60 years of age by cause per 1,000 population [11]
2.2 Treatment of HIV/AIDS

The first methods of treatment were introduced in 1987 in the form of ARV drugs and by 1996 treatment of the virus progressed to a triple combination of ARVs, which became known as Highly Active Antiretroviral Therapy (HAART) (Section 3.3 covers this area in greater detail). In the three years following the introduction of HAART the rate of AIDS related mortality was reduced by 60 to 80% [12].

Today a cure for AIDS is still absent but the disease is treatable via HAART. Unfortunately HAART has been mainly confined to the developed countries, as individuals in developing countries cannot afford the high priced brand name drugs. In 2003 there were between 4 and 8 million people in need of ART. However, only 7% of the people who were in need of ART in developing countries were receiving it [15]. This situation is slowly changing with the introduction of initiatives such as the United Nations (UN) 3 by 5 initiative, which aims to have 3 million people who need ARVs on ART by the end of 2005[13]. Also the production and introduction of generics has reduced the cost of ARVs, making the drugs more accessible to people who need them. In Uganda, 40mg of brand name d4T drugs fell from US$173 per month in December 2000 to US$23 per month in February 2001. This drop in price continued and by April 2002 the cost was US$6 per month [14].

The problem of HIV/AIDS is multifaceted. One aspect that needs to be addressed in solutions to this complex problem is health service capacity. Sub-Saharan Africa is not only badly affected by HIV/AIDS but also has limited health service capacity.

2.3 Effect on Sub-Saharan African Health Systems

With the increase in availability of antiretroviral drugs in sub-Saharan Africa, the lack of HCWs, adequately trained in the administering of ART has been highlighted. Traditionally the shortage was attributed to the high number of losses to other occupations and developed countries, however HIV/AIDS has compounded the problem even further. Figure 4 illustrates this point by showing the number of HCWs who have been lost to HIV in Malawi.
Production of new HCWs has also been curtailed here by the disease. 110 newly trained nurses were added to the health system between 1997 and 1998. But taking into account that 44 nurses were lost to HIV/AIDS the actual number added to the health system was a maximum of 66. This problem was further compounded in sub-Saharan Africa with the loss of educational professionals to the disease, thus reducing the ability for the training of new health professionals. A high rise in absenteeism has also been attributed to the disease. According to the 2004 World Health Report, in Malawi laboratory workers are absent nearly half of their total working time because of HIV/AIDS [15]. The result of this is that the remaining HCWs are being left to deal with the growing number of cases. These cases tend to require intensive care and mortality can be high which can lead to the demoralisation of the HCWs [16].

In Uganda the training of healthcare workers is further complicated by the structure of the existing healthcare system which has many different levels of clinics. At the highest level the clinicians are well trained but at lower levels the HCWs may not have any healthcare training.

### 2.4 The Ugandan Health System

Uganda has an estimated population of over 25 million which is growing at over 2.5% per annum. It is one of the few sub-Saharan African countries experiencing a reduction in HIV prevalence (30% in 1983 down to 6% in 2003). This has been attributed to an increase in the population’s awareness of the disease to nearly 98% [17].
However, Uganda still experiences 100,000 new cases of HIV a year. 30,000 babies are born HIV positive each year through mother to child transmission (MTCT) – something that is largely preventable should the mother be given the correct treatment. Roughly 2.2 million Ugandans have been infected with the virus and 1 million of these have died. The health system is severely under pressure due to the disease with 40% of hospital beds and 80% of TB wards being filled with HIV/AIDS patients [17].

The Ugandan Health system consists of seven layers. At the highest level are national hospitals such as Mulago and Butabika. Below the national hospitals are regional hospitals. Regional hospitals include all services that are expected from a hospital as well as some specialised services. District hospitals follow regional hospitals in the health structure. There are currently 56 district hospitals in Uganda whose facilities include well-equipped theatres. Following district hospitals are county hospitals. County hospitals consist of a theatre(s), which is equipped for emergencies such as road traffic accidents. Voluntary Counselling and Testing (VCT) also exists in 30% of the clinics at county level and by 2010 it is planned to raise this level to 100% [18]. At sub county level there are no operating theatres. The staff here must include at least one midwife, two nurses - where one is a comprehensive nurse*, and a clinical officer. The clinical officer is in charge of the clinic but in the majority of cases a midwife fulfils the role of clinical officer. The two most basic levels of the system are known as parish level and village health committee. A parish level clinic is operated by a nurse or in some cases two nurses. One of the functions of this type of clinic is to administer the treatment of Infectious diseases. The lowest level of clinic found in Uganda is the village health committee and this type of clinic tends to be run by HCWs who have not received formal healthcare training. At this level it is often necessary to refer patients to higher-level clinics. In these cases the decision as to where the patient is referred to is based on the distance from a clinic with the required facilities [19].

2.5 Summary

This chapter has described the domain of HIV/AIDS. Statistics relating to the burden that the disease places on the world have been presented. From these statistics it has been identified that sub-Saharan Africa is carrying the majority of the burden. The chapter also outlined the impact that the disease is having on the health systems of this region. Finally a description of the UHS

* A nurse trained in both midwifery and general nursing.
was provided in order to give the reader an understanding of the range of skills and facilities available at the different types of clinic in Uganda.

The following chapter HIV/AIDS provides a summation of the virus’ life cycle. It also gives a description of the various different stages that a HIV positive person goes through together with an account of the treatment methods that are currently available. This is followed by a description of the recommended treatment regimens for Uganda.
3 HIV/AIDS

This chapter provides a concise overview of the virus’ life cycle. This is followed by an outline of the different stages that a patient infected with HIV/AIDS goes through. The chapter also informs the reader of the different classes of ARVs which exist. Finally the recommendations for combining these classes of ARVs in Uganda are provided.

3.1 Life Cycle of the HIV Virus

Viruses are microscopic infective particles. They have no metabolic machinery and must attach themselves to a host in order to survive and replicate [20]. The HIV virus is an RNA (Ribonucleic Acid) virus, which selectively infects the T lymphocyte cells called CD4 cells (also known as T helper cells). After attaching itself to the host cells’ CD4 receptors (stage 2 of Figure 5) the virus penetrates the cell membrane and begins a process of replication. During replication the virus’ genetic material, RNA undergoes reverse transcription leading to it being converted into viral DNA (stage 4 of Figure 5). In order for this process to occur the enzyme Reverse Transcriptase is necessary. As a result of reverse transcription, viral DNA enters the cells nucleus where it is incorporated into the hosts’ genome* [21]. This causes the cell to produce new viral components, which may remain latent for many years and because of this, it is necessary for a patient receiving ART to remain on ART for the rest of their life. When the virus is active, the viral components are assembled into a new virus outside the nucleus at the cell membrane (stage 7 of Figure 5). A vital viral component in this process is a protein called protease. ARVs called protease inhibitors prevent protease from functioning and therefore the virus is prevented from becoming fully mature. The new virus buds from the CD4 cell where it is “cleaved” from the cell before moving on to infect another cell (stages 8 & 9 of Figure 5) [22], [23], [24]. Eventually the process of viral replication increasingly dominates the host cells’ activity, which ultimately leads to its destruction.

* The genetic information contained in one complete set of chromosomes
Due to the amount of replication that occurs, mutations resistant to ARVs occur. In cases where administration of ARVs is not carried out correctly or patient adherence is poor the likelihood of resistance is greater [25].
3.2 Stages of HIV/AIDS

It is important to distinguish between the various stages that the HIV/AIDS virus goes through, as each phase can have a different effect on the patient. The first stage, *viral transmission*, can occur through sexual intercourse, exposure to contaminated blood, breast feeding, or by MTCT. Following viral transmission, in approximately fifty to ninety per cent of cases the patient experiences *symptomatic primary HIV infection*. This period tends to commence between two and four weeks after the initial exposure and can last from one to four weeks however the average is two weeks. Due to the range of symptoms that can occur at this stage, diagnosis of HIV/AIDS is often missed. During symptomatic primary HIV infection the patient experiences a decrease in their CD4 count as illustrated in Figure 6. The extent to which the CD4 count is reduced is influenced by the opportunistic infections (OIs). In contrast while there is a reduction in the CD4 count the viral load increases giving a mirror image effect. After around three weeks the viral load count (VLC) increase, peaks and from this point it decreases. This reduction in viral load occurs at the same time as the CD4 count begins to increase. Following symptomatic primary HIV infection the patients’ viral load decreases and their CD4 count increases again but it rarely reaches the previous high levels [12].

![Figure 6: Graph showing the correlation between CD4 and Viral load levels](image)

Most patients seroconvert (develop antibodies to the virus [27]), four to ten weeks after exposure and over ninety five percent convert after six months. During *seroconversion* the viral load begins to stabilize and by six months it remains at a constant level or it starts to slowly increase again over a long period of time without ARV drugs. After six months the patient enters the *clinical*
latent period. During this time they are asymptomatic of HIV/AIDS except in some cases where they may experience lymphadenopathy (enlargement of lymph nodes [28]). This phase can extend beyond eight years and such cases are known as “Chronic non-progressors” [12].

When a patient’s CD4 count drops below 200/mm3 they are considered to have AIDS. Without ART their CD4 count will continue to fall and when it drops below 50/mm3 the patient is in an advanced HIV infection stage. If ART were not provided at this stage the maximum survival period would be up to 18 months.

### 3.3 Antiretroviral Therapy

A number of classes of ARVs exist, each targeting the HIV virus at a different stage of its life cycle. The group of ARVs consists of Protease Inhibitors (PIs), Entry Inhibitors, Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and Integrase Inhibitors. Table 1 provides a selection of common PIs, NRTIs and NNRTIs. Examples of entry inhibitors, also known as fusion inhibitors, and integration inhibitors have been omitted as their use is largely confined to developed countries due to their cost.

Current ART methods consist of prescribing a patient with a combination or ‘triple tonic’ of ARVs commonly referred to as HAART. Monotherapy with any of these ARVs leads to a rapid selection of mutations of the virus which are resistant to the drug. HAART is composed of either an NNRTI or a Protease Inhibitor along with two NRTIs. Together the combined ARVs can have a synergistic effect on each other when combating resistance. For example variant resistant to the NRTI AZT may begin to develop resistance against 3TC. However as it’s resistance to 3TC grows it can become less resistant to AZT [29].

PIs prevent infected T-Cells from producing new copies of the HIV virus by blocking viral assembly [30] by preventing HIV protease from cleaving polyprotein precursors from a HIV infected cell. As a result of the protease inhibitors intervention an essential stage of the HIV virus life cycle is rendered incomplete leading to the production of an immature and therefore non-infectious cell [31].

There are two types of NRTIs, Nucleotide Reverse Transcriptase Inhibitors (also referred to as Nucleotide Analogues) and Nucleoside Reverse Transcriptase Inhibitors (Nucleoside Analogues). Currently there is only one approved Nucleotide Analogue available with the rest of the NRTIs
being Nucleoside Analogues. Nucleotide Analogues differ from Nucleoside Analogues in that the former are chemically active when they enter the body whereas the latter are not and must undergo a chemical change [32].

NRTIs use faulty versions of Nucleotides which are used by reverse transcriptase to convert RNA to DNA. When reverse transcriptase uses these faulty Nucleotides, the DNA that is formed from the building process is defective and therefore the HIV genetic material is immiscible with the cell’s DNA, which means that the cell does not produce anymore of the virus.

NNRTIs are also known as Non Nucleoside Analogues. NNRTIs bind to the enzyme reverse transcriptase and by doing so prevent it from creating DNA from the RNA which would be mixed with the T-Cells healthy DNA.

<table>
<thead>
<tr>
<th>Protease Inhibitors</th>
<th>NNRTIs</th>
<th>NRTIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir/Ritonavir</td>
<td>DLV (Delavirdine)</td>
<td>AZT (Zidovudine)</td>
</tr>
<tr>
<td>IDV (Indinavir)</td>
<td>EFV (Efavirenz)</td>
<td>ddl (Didanosine)</td>
</tr>
<tr>
<td>ATV (Atazanavir)</td>
<td>NVP (Nevirapine)</td>
<td>ddl-EC (Didanosine EC)</td>
</tr>
<tr>
<td>APV (Amprenavir)</td>
<td></td>
<td>ABC (Abacavir)</td>
</tr>
<tr>
<td>NFV (Nelfinavir)</td>
<td></td>
<td>3TC (Lamivudine)</td>
</tr>
<tr>
<td>RTV (Ritonavir)</td>
<td></td>
<td>TDF (Tenofovir)</td>
</tr>
<tr>
<td>SQV (Saquinavir)</td>
<td></td>
<td>FTC (Emtricitabine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ddC (Zalcitabine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>d4T (Stavudine)</td>
</tr>
</tbody>
</table>

Table 1: Selection of Available ARVs [33]

3.4 Administration of ART in Uganda

It has been previously mentioned that the treatment of HIV can be composed of two NRTIs and either a protease inhibitor or an NNRTI. In Uganda, the recommended first line regimen usually consists of two NRTIs and an NNRTI. The option of a protease inhibitor is left for cases where first line therapy fails [37].

A patient should only commence ART once they have completed VCT. The guidelines for Uganda and other developing countries also state that the CD4 count should be less than or equal to 200/mm³ before commencing ART. However, in cases where the patient is clinically diagnosed
with a WHO stage IV disease (Appendix 2 – WHO Stages) or alternatively a WHO stage III disease with persistent/recurrent oral thrush along with invasive bacterial infections a CD4 cell count is not necessary. The Ugandan guidelines also recommend that patients who are diagnosed with Tuberculosis commence ART with a CD4 count of 350/mm$^3$ or under [37].

It is important to note that ART also can be seen as a preventative measure against the spread of HIV/AIDS as it reduces the viral load presence in the patient, therefore making them less infectious [34].

### 3.5 Summary

This chapter provided a description of the life cycle of the HIV virus. The stages that a HIV positive patient goes through were also identified along with the current treatment methods that exist for HIV. Finally the Ugandan indications for commencing ART were outlined.

The next chapter introduces the reader to CPGs. This is followed by a review of a number of methods which exist for capturing them electronically namely GLIF, UML, PLAN and Arden Syntax. An overview of the clinical coding of HIV/AIDS in ICD-9 and ICD-AM-10 is also provided. Finally clinical data which is required in order for a HCW to recommend an ARV regimen given.
4 Guidelines & Coding schemes

This chapter provides an introduction to clinical practice guidelines (CPGs). This is followed by a review of a selection of specifications that are available for representing CPGs electronically. The reader is then presented with a summary of the proposed method for linking CPGs and patient data – clinical coding. Particular attention is paid to the clinical coding of HIV/AIDS when using the coding schemes ICD-9 and ICD-10-AM. Finally, clinical data required to create a CPG for treating HIV/AIDS that was extracted from the Ugandan guidelines is presented.

4.1 Clinical Practice Guidelines

CPGs can be described as “clinical knowledge that is used to ensure and improve quality of healthcare, to reduce inappropriate variations in clinical practice and healthcare costs, used for medical education, alerts and reminders, case management and decision support” [35]. A more concise definition offered by Hederman et al defines CPGs as “recommended strategies for patient care” [36].

Currently the Ugandan Guidelines for HIV are finalised in a text based format. The guidelines were written by numerous national experts in the domain of HIV/AIDS and were edited by Prof. Elly T. Katabira and Dr. Moses R. Kamya along with members of the Clinical Case Subcommittee and the Ministry of Health (MoH) [37]. A well documented deficiency with text based CPGs is that they are difficult to incorporate into clinical work practices and therefore their impact on a clinician’s work habits are minimal [35], [36], [38], [39], [40]. One solution to this problem is to convert CPGs into an electronic format which can be interpreted by a computer. Then by linking the computable CPGs with the EPR it is easier to incorporate the CPGs into work practices thus leading to a greater level of compliance [39]. The following sections (4.2 and 4.3) present two potential approaches for representing CPGs in electronic format namely a process oriented approach and a rule based approach.
4.2 A Process Oriented Approach

This section provides an overview of two process oriented approaches to representing CPGs, Guideline Interchange Format (GLIF) and Unified Modelling Language (UML).

4.2.1 Guideline Interchange Format

GLIF is a guideline specification that was developed by Stanford Medical Informatics, the Decisions Systems Group of Brigham & Women’s hospital, Harvard Medical School, the Department of Medical Informatics at Columbia University and the Center for Medical Education at McGill University. GLIF was developed to allow for the sharing of computer interpretable clinical guidelines between medical institutions [36], [41].

The GLIF specification is currently in its’ third version which is known as GLIF3. GLIF3’s predecessor GLIF2 was first published in 1998. It allowed for the specification of a guideline as a flow chart which modelled the clinical decisions and action steps of clinical guideline. GLIF2 was implemented in Brigham’s Brigham Integrated Computing System (BICS) but proved difficult to integrate into clinical systems due to the absence of a mechanism for linking GLIF2 to an EPR [41]. Further deficiencies of GLIF2 which have since been addressed in GLIF3 consisted of a lack of descriptions for items including, the current state of the patient, iteration and exceptions [42].

GLIF3 allows for the specification of guidelines at three different levels. These levels consist of:

a) The conceptual level.

b) The computable level.

c) The implementable level.

At the conceptual level the guideline is in the form of a flowchart (e.g. Figure 7) which is used for browsing but not for decision support. At the computable level the guideline is verified for consistency and completeness. Patient data types are also defined at this level along with the possible clinical actions. The final level, implementable, is the actual guideline which is incorporated into an organisation. It is tailored to a specific organisation and as a result it may contain non-shareable items [41].
Like its’ predecessor GLIF3 is composed of a GLIF model and GLIF syntax. The GLIF syntax is in XML format and it complies with the resource description framework (RDF) schema [42]. The GLIF model consists of:

a) A set of classes for guideline entities.
b) Attributes for the classes.
c) Data types for the attribute.

Each guideline object is made up of a list of authors, a description of the guideline’s intentions, patient eligibility criteria, a list of supporting references, the starting point of the guideline, and an unordered list of steps [43]. There are five different types of steps (illustrated in Figure 7) accounted for in the specification, 1) the action step, 2) the decision step, 3) the branch step, 4) the synchronisation step and 5) the patient state step [42]. These steps comply with the modelling primitives and constructs shown in Table 2 which were deemed necessary for guideline representation by Wang et al [44].

<table>
<thead>
<tr>
<th>Modelling Primitives &amp; Constructs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decisions</td>
</tr>
<tr>
<td>Actions</td>
</tr>
<tr>
<td>Patient State</td>
</tr>
<tr>
<td>Scheduling Constraints</td>
</tr>
<tr>
<td>Nesting</td>
</tr>
</tbody>
</table>

Table 2: Modelling Primitives and Constructs for guideline representation

Action steps refer to tasks that are to be performed and are represented by a rectangle. There are two different types of decision steps, choice and case. A case step (diamond shape) differs from a choice step as it is automated where as a choice step (hexagonal) must be confirmed by a user. Branch steps model concurrent guideline steps. Finally the patient state (oval) symbolises the entry point of the patient into the guideline or particular milestones that the patient has reached [36].
The components found in the GLIF3 model are similar to those found in activity diagrams which are part of the mainstream modelling language, UML. These similarities were explored in a Higher Education Authority (HEA) funded project called MediLink [36].

4.2.2 Unified Modelling Language
MediLink was an inter-institutional, inter-disciplinary project involving Trinity College Dublin (TCD), Dublin Institute of Technology (DIT) and SJH which was concerned with developing protocols of care and linking and applying medical knowledge to patient records with the overall aim of improving quality of care. One element of the MediLink project investigated the use of mainstream business modelling technology to model clinical guidelines using a process oriented
approach. The resulting model known as an *enactable CPG* could then be executed by a Workflow Management System (WfMS). By using mainstream technology it was felt that it would be easier to take advantage of advances in WfMSs as opposed to being restricted to enactment tools which were specifically designed for a particular guideline [35]. There are 5 main parts to a process oriented design which consist of, actions, decisions, branches, synchronisation steps, and patient states. [36][44].

MediLink’s chosen modelling language was the defacto modelling language used by the I.T. industry to model workflow processes, UML. UML describes how activities/processes are coordinated using activity diagrams [45] which include all of the components required by a process oriented approach (see Table 2).

The activity diagrams were created manually on paper or electronic files by a clinician from assessing a text based guideline. This was the only manual part of the entire process with the rest being performed electronically. The UML activity diagrams were enacted producing dynamic clinical guidelines which were in the form of Xml Metadata Interchange (XMI). XMI is UML’s eXtensible Markup Language (XML) model description interchange format. The XMI was then converted to interpretable rules through the use of Extensible Stylesheet Language Transformations (XSLT). These rules formed the care process knowledge and were applied to an e-Clinic which identified unstable diabetic patients based on the results of home glucose tests [35], [38].

### 4.3 A Rule Based Approach

An alternative approach to process oriented guidelines is rule based guidelines. Two rule based architectures PLAN and Arden Syntax, which are used to implement electronic clinical guidelines are presented in the following section. Both of these approaches applied an ECA (Event Condition Action) rule based mechanism.

ECA rule mechanisms are well established in the database community [48]. The semantics of an ECA rule is that when an event occurs; if certain conditions are met then specified actions are executed [46] [47]. ECA rules can be described as being comprised of three components: events, conditions and actions. An event describes the incident that makes the rule relevant. Examples of possible events described by Wu [46] for a clinical test request protocol include a passage of
time, abnormalities in the patient’s condition, problems that may develop during the treatment of the patient or any combination of these events. Conditions determine the situation in which the rule can be applied. Actions outline the task(s) to be carried out should the event and its associated conditions be valid.

### 4.3.1 PLAN

PLAN is a generic modelling framework created by DIT, which implements an ECA mechanism for clinical test request protocols [48]. Table 3 outlines the ten main concepts of this specification.

<table>
<thead>
<tr>
<th>Concept</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Protocol Management System</td>
<td>System that creates, stores, executes and manages a set of test request protocols.</td>
</tr>
<tr>
<td>Test Request Protocol</td>
<td>Generic plan for ordering clinical tests for a particular patient category. Contains a Base Schedule. Contains a set of protocol rules.</td>
</tr>
<tr>
<td>Base Schedule</td>
<td>Series of clinical tests to be ordered. (See Figure 8).</td>
</tr>
<tr>
<td>Patient Test Plan</td>
<td>Plan for ordering a set of tests for a patient within a particular category. Instance of a test request protocol relevant for a particular patient.</td>
</tr>
<tr>
<td>Protocol Rule</td>
<td>ECA rule that dynamically monitors a Base Schedule and intervenes to order actions. Accounts for nearly all possible events, conditions and actions. (See Figure 9).</td>
</tr>
<tr>
<td>Static Rule</td>
<td>ECA rule to order tests based on a time. Conditions are always true. Actions are mainly confined to clinical test orders.</td>
</tr>
<tr>
<td>Dynamic Rule</td>
<td>Instance of a protocol rule which is contained in a patient test plan.</td>
</tr>
<tr>
<td>Event</td>
<td>Occurrence of something defined with a particular domain. Events are based on time and the patients well being.</td>
</tr>
<tr>
<td>Condition</td>
<td>A stipulation that must be fulfilled. Conditions are based on the EPR and test results.</td>
</tr>
<tr>
<td>Action</td>
<td>The result of a condition or a number of conditions.</td>
</tr>
</tbody>
</table>

Table 3: Main Concepts of PLAN [46]
PLAN places patients into categories and sub-categories for purposes of clinical test ordering. Each of these categories has a generic test-ordering protocol assigned to it which consists of a base schedule and a set of protocol rules. The set of protocol rules along with the set of schedules can interact with each other depending on actions triggered by specific events. Only one dynamic rule can be assigned to a patient category and its function is to monitor the actions of a static rule or a set of static rules and act on them. Dynamic rules also monitor the state of the patient. Where changes occur to the patient’s state, actions are invoked. These changes may be indicated by test results or other types of measurement in addition to changes in the patient condition [48] [46] [49].

<table>
<thead>
<tr>
<th>RuleName: schedule_rule_1</th>
<th>RuleName: protocol_rule_1</th>
</tr>
</thead>
<tbody>
<tr>
<td>RuleType: static</td>
<td>RuleType: protocol</td>
</tr>
<tr>
<td>RuleStatus: active</td>
<td>RuleStatus: active</td>
</tr>
<tr>
<td>StartTime: check_in_day</td>
<td>On test_result{K}</td>
</tr>
<tr>
<td>On day{-1, 0, 1, 2, 3, 4, 6, 8, 11, *3}</td>
<td>IF K &gt; 5.5 or K &lt; 3</td>
</tr>
<tr>
<td>Do order_test{U &amp; E}</td>
<td>Do order_test{U &amp; E}</td>
</tr>
</tbody>
</table>

**Figure 8: A base schedule rule [49]**

**Figure 9: A protocol rule [49]**

Each clinical protocol is written to a text file. The text file is parsed and its’ attributes are stored in a relational database. Using a relational database allows for querying and manipulation of these attributes which is not possible with other attempts to apply ECA rule mechanisms such as the Arden Syntax [48]. PLAN is implemented in a decision support system called TRiPS in Tallaght Hospital.

### 4.3.1.1 TRiPS

TRiPS is a rule based decision support system responsible for issuing reminders to clinicians to order certain tests or test profiles. These reminders are based on pre-specified times or as a response to abnormal test results, the consequence being a reduction in the volume of data that a clinician would have to review in order to make the same decision.

The particular application of TRiPS investigated as part of this dissertation screens plasma glucose results for potential new cases of diabetes mellitus. In doing so, patients who have not been diagnosed with diabetes and are not suspected as being diabetic can be diagnosed at an earlier stage.
TRiPS, uses a Common Object Broker Request Architecture (CORBA) naming service to locate the various sources of information. Patient demographics are retrieved from the PiMS database. Information about patients who have been previously diagnosed as diabetic is taken from a system called Diamond and previous test results are retrieved from the OCS. Also, the results from lab tests are taken from the hospital’s Integration Engine (IE) which is responsible for converting DOS formatted data into a format which is usable by other applications. TRiPS was programmed with a generic approach and the result is that due to the amount of data taken in by TRiPS it could be extended to screen for other tests such as thyroid function tests provided a rule based approach could be applied.

The TRiPS application operates by screening the results from the IE to detect any abnormal results. This process is based on two different screening protocols (OGTT tests and RGT or FGT) which have rules assigned to them. The positive test cases are temporarily kept on the ‘screen test plan’ before being manually transferred to the diagnosis protocol. Positive results pass through the counteractive protocol which ensures that the patient is not already on the Diamond system. The counteractive protocol also assesses other details such as the current state of the patient (e.g. whether they have died since the sample was taken). The outcome of cases passing through the counteractive protocol is that only positive results that need to be transferred to the diagnosis protocol are passed on.

Once a patient has entered the diagnosis protocol, any symptoms that they may have are recorded. A list of actions to take are also provided, some of which include moving the patient to the Diamond system, order a random plasma glucose (RPG), order a fasting plasma glucose (FPG), or order a glucose tolerance test (OGTT). The final three actions most often refer to a confirmation test, which must be of the same type as the previous test. All confirmation tests must be conducted within 6 months [50].

4.3.2 Arden Syntax
The development of the first Arden Syntax began in 1989 with the aim of creating a methodology which allowed for the sharing of medical decision rules across different medical institutions and platforms. In 1992 the first version was published as a standard which was accredited by the ASTM (American Society for Testing and Materials). The second version which followed later was published under an ANSI accredited standard, Health Level 7 (HL7) [51].
Arden Syntax encodes medical decision rules in the form of Medical Logic Modules (MLMs) (Appendix 1 – Example of Arden Syntax). Each MLM encapsulates components such as the event that triggers the MLM, which are necessary to make a single decision. These components are selectively placed into slots of three different categories, maintenance, library and knowledge.

The maintenance category is used for knowledge base revision and control while the library category provides clinical information and references to the literature. The knowledge category contains the slots evoke, logic and action which relate to the ECA rule components event, condition and action. There is also a data slot which separates institution dependent information such as the location of clinical data from the rules [51]. The data slot also introduces the ‘curly brackets’ (‘{}’) problem. This problem relates to the absence of a standard for retrieving data from the EPR and all the data inside the ‘curly brackets’ is institution specific.

4.4 Clinical Coding of HIV

As this dissertation explores the application of clinical codes as a means for providing a link between CPGs for HIV/AIDS and an EPR it is necessary to review how the disease is currently coded. This section introduces the different levels of clinical coding that exist which leads into a description of how HIV/AIDS is coded in ICD-9 and ICD-AM-10.

In an ‘Analysis of an Electronic Future of Clinical Coding’, King describes the three levels of clinical coding that exist. The first level of coding relates to each diagnosis associated with a patient. The clinical coding scheme ICD-9 provides the individual codes for diseases and procedures in Ireland and is currently being upgraded to ICD-10, which has an even greater depth of codes.

The second level of coding described by King involves grouping patients’ diseases and procedure codes into a code. This grouping known as Diagnostic Related Group (DRGs) is based on patient specific data and diagnostics that use similar resources. The highest level of coding consists of Major Diagnostic Code (MDCs), which consist of DRG codes, and corresponds to an organ system. It is important to note that this grouping of codes leads to a loss of detail and the result is that with a higher level of coding less information is available.
Allocating codes against patient information is known as Casemix. In Ireland the main use of these codes is for allocating funding to a hospital, however France has identified other uses, which include measuring productivity and benchmarking for quality of care [52].

4.4.1 ICD-9

ICD-9 consists of 6 codes directly related to HIV/AIDS namely 042, V08, 795.71, V69.4, V73.89 and 647.6X. Only cases that are confirmed as being related to HIV are coded with these codes. To establish HIV status and commence ART, the current CPGs require a laboratory confirmation; however for coding purposes a physician’s diagnostic statement is sufficient.

When a patient is admitted with a HIV related condition the principal diagnosis code given is 042 followed by additional codes for other diagnoses. In cases where the patient is admitted for a case unrelated to HIV but is HIV positive the principal diagnosis code is not 042 but rather the code for the cause of the patient’s episode. 042, in these cases is entered as an additional diagnosis followed by other additional diagnosis codes.

V08 is applied to cases where the patient is asymptomatic of HIV and is without documentation. The code can only be assigned once and is not used in AIDS related cases or where the patient has been previously treated for HIV related illnesses or has been previously described as having conditions resulting from HIV. In these cases 042 is assigned.

The code 795.71 is assigned to cases where the HIV serology test is inconclusive. The patient must have no definite diagnosis of HIV or no manifestations of the disease. If the patient has been previously assigned 042 it cannot be used.

During pregnancy, childbirth or puerperium 647.6X is assigned followed by 042 or V08 depending on whether the case is HIV related. V69.4 is assigned to patients who are entering counselling and V73.89 is assigned to patients who are waiting for their HIV status to be determined [53].

4.4.2 ICD-10-AM

ICD-10-AM is the Australian version of ICD-10 and it will be implemented in Ireland in 2005. In this coding scheme there are seven codes that are directly associated with HIV/AIDS. They
consist of R75, Z21 and B20 to B24. Each code is mutually exclusive and should not be listed together.

R75 is assigned to patients whose tests for HIV are inconclusive. It is never assigned as a principal diagnosis and usually is assigned when the screening test is positive but the confirmatory test is negative or inconclusive. Usually the patient is tested again to obtain a definite test result.

The code Z21 is assigned to patients who are admitted but not for HIV related issues. It relates specifically to patients who are asymptomatic and have not been diagnosed as being HIV positive. As the reason for admittance is never HIV related the code is never assigned as the principal diagnosis.

B23 is assigned to patients who are at the Acute HIV Infection Syndrome stage of the virus. Again this code is never assigned as the principal diagnosis and it is never assigned twice as the patient passes through this stage quickly.

Codes B20 to 24 are assigned to patients who develop manifestations that may or may not be AIDS defining. These codes are assigned as the principal diagnosis if HIV is the main cause of the patient’s manifestation. In cases where they are not the main cause of the condition then the code of the manifestation is assigned.

There are other non-HIV codes that have been explored during this dissertation which relate to important aspects of the disease. Codes such as Y41.5 which, relates to an adverse side effect caused by ARVs will also play a major role in this application.

Essentially the main difference between ICD-9 and 10 from a coding prospectus is that ICD-10 introduces an alphanumeric coding scheme to replace a numeric scheme. This offers a more comprehensive coding scheme than its predecessor with over 4,000 more categories available [54].
4.5 Clinical Data

Following a review of the Ugandan guidelines for ART the data items listed in Table 4 were identified as essential components of the EPR in order to provide a recommended regimen for ART.

In the majority of cases a CD4 cell count is required to commence ART. Situations where a CD4 count would not be required include: if the patient is co-infected with extra-pulmonary TB or a WHO stage IV disease. See section 3.4 for further details. Additionally a patient’s haemoglobin (Hb) count is required in order to determine whether a patient is anaemic. Patients who are anaemic are unable to commence ART. The last five data items listed in Table 4 are used to help to determine whether a patient is contraindicated to a particular regimen. Finally the data item viral load is used to assess the aggressiveness of the disease. However viral load tests are uncommon in resource deprived areas due to the cost of conducting one and therefore is not essential.

<table>
<thead>
<tr>
<th>Data Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases that the patient has/had which are</td>
</tr>
<tr>
<td>symptomatic of HIV/AIDS</td>
</tr>
<tr>
<td>The WHO Stage of a disease</td>
</tr>
<tr>
<td>CD4 cell count</td>
</tr>
<tr>
<td>Viral load</td>
</tr>
<tr>
<td>Hb level</td>
</tr>
<tr>
<td>Pregnancy Status</td>
</tr>
<tr>
<td>Previous Psychiatric illnesses</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Current and previous medication</td>
</tr>
</tbody>
</table>

Table 4: Data items which are essential in order to recommend an ARV regimen
4.6 Example of ICD Codes Being Applied in CPGs

The following paragraph is a sample case which is used to illustrate how a link between CPGs and an EPR could be provided through ICD-10 codes:

A 23 year old man comes to the clinic with a cough of six weeks duration. At present he weighs 56 kg but has lost 11 kg over the last month. Diagnosed with pulmonary tuberculosis, he is taking Rifampicin. The tuberculosis clinic performed a CD4 test and his CD4 count is 209. In addition he has suffered from oral candidiasis within the last year.

From this short case the data items of notable interest which can be extracted include:

- Weight: 56Kg
- Age: 23
- CD4 count: 209
- Diagnoses: Pulmonary Tuberculosis (A16.2), severe weight loss, oral candidasis/oral thrush (B37.0)
- Medication: Rifampicin

Table 5 gives an example of an ICD-10 code providing a link between patient data and CPGs which are in an ECA format. In this instance if the code for pulmonary tuberculosis, A16.2, is found in the EPR and the patient has a CD4 count between 200 and 350 while they are also taking Rifampicin the message assigned to alert_text will be displayed.

```plaintext
logic:
    elseif
        checkDisease("A16.2") = true and (last_CD4 > 200 and last_CD4 < 351 or hasStageIVDisease() = true) and pregnant = false and checkDrug("rifampicin") = true
    then
        alert_text := "Start TB Therapy for 2 months THEN start one of these regimens: AZT/3TC/EFV or d4T/3TC/EFV";
```

Table 5: Extract from coinfections MLM illustrating the use of ICD codes as a means for linking patient data with CPGs
4.7 Summary

This chapter has introduced the topic of CPGs and the different methods available for representing them electronically. A summary of the proposed method for linking CPGs with patient data – clinical coding, was also described which included an overview of how HIV/AIDS is coded using the coding schemes ICD-9 and ICD-10-AM. Finally, clinical data required to create CPGs for treating HIV/AIDS which was extracted from the Ugandan guidelines was described. The next chapter introduces the novel approach of using mobile technology as a means for distributing CPGs for HIV/AIDS.
5 Assisting Healthcare Delivery in Under Resourced Areas

In the absence of basic healthcare facilities and resources it is questionable as to whether resources should be allocated to ICT in the fight against the spread of HIV and other infectious diseases. However the G8 Digital Opportunity Task Force (DOT Force) suggests that through the use of ICT it is possible to offer tools which lend themselves to improved knowledge development and information sharing [55].

ICT can take many forms and is not confined to internet based technologies. In fact internet coverage in Africa is only available to 0.1% of the African population with half of that amount having access. Currently the forms of ICT which have the greatest coverage in Africa consist of Television (40%) and Radio (75%) [55].

Health facilities, especially in isolated rural communities, are struggling to keep workers for reasons described earlier in section 2.3. The remaining HCWs are left to operate in isolation of their peers and up-to-date clinical information. This is seen as a contributing factor for the reliance on traditional medicines and the lack of uptake of modern practices in Africa [55].

ICT has the potential to reduce the level of isolation experienced by rural HCWs by providing a tool which facilitates the spread of information relating to the treatment of the HIV/AIDS. PDAs are one form of technology that has been proven in pilot projects such as Satellife and Ca:sh to facilitate the spread and analysis of information at even the lowest level in the health systems. This chapter provides an introduction to PDAs which includes a comparison between Pocket PCs and Palm PDAs. Additionally accounts of projects where PDAs have been deployed in resource starved health systems are given. Design issues to be considered when creating an application for a mobile device are also outlined. Finally important features of the programming language J2ME which is tailored for mobile devices are described.

5.1 Personal Digital Assistants

A PDA also known as a handheld computer is a mobile device which the user interacts with by tapping on the screen with a stylus. A PDA can facilitate applications for email, web browsing and viewing documents and spreadsheets. Data can be input by tapping the onscreen keyboard or by writing on the screen with the stylus. In the latter case an application such as Graffitti converts
the handwriting to text format. Other peripherals can be added to the PDA such as keyboards to allow for data input. There are two main categories of PDA. Palm OS based and Windows based (Pocket PC) [56].

5.2 Palm vs Pocket PC

The majority of PDAs are hosted by either Palm OS (Operating System) or Windows CE, with a small number having Linux as their OS. The main Palm OS based PDA manufacturers consist of Palm, Sony and Handspring while Hewlett Packard, Dell and Toshiba are responsible for the production of most of the Windows CE based PDAs. To date Palm OS has the larger market share of the two but this market share is gradually being reduced. In a study into healthcare applications for PDAs by Yen-Chiao et al, it was identified that more applications were available to Palm PDAs than Windows [56]. Another advantage offered by Palm based PDAs, which is important considering the chosen domain, is that Pocket PCs are more expensive than Palm PDAs. Palm PDAs also provides a battery life that is much longer than a laptop or a Pocket PC [56]. This attribute is essential in parts of Africa where there is no guaranteed electrical supply. However small solar panels exist which facilitate the charging of a PDAs battery and therefore battery life is less of an issue when comparing Pocket PCs and Palm PDAs [18].

PocketPCs offer greater functionality and the majority of them come with WiFi (Wireless Fidelity) and Bluetooth installed. To date there is no Palm with both of these technologies installed on the one PDA although it is possible to install WiFi onto a Palm using a WiFi SD card. Also most Pocket PCs come with compact flash slots as well as SD slots whereas to date the only Palm that comes with both is the Tungsten T5. The advantage of the compact flash slot is that there are more peripherals such as cameras available for compact flash.

5.3 The Role of PDAs in Healthcare

Mobile technology in the field of healthcare is becoming more cost effective and common [39] and in particular the use of PDAs has risen sharply [57]. One example of PDAs being successfully applied in healthcare is given by Fu et al [39], which describe a pilot project in China that uses PDAs to collect and transfer patient data to a central database. The project also facilitated the transfer of electronic CPGs. Another example described in ‘Using PDAs for Data Collection’ [57] illustrates how PDAs were used to collect data in emergency departments on elderly patients who showed signs of neglect.
Some of the potential benefits that mobile technology offers to a HCW identified by these projects, include access to clinical information and decision support at the point of care, facilitation of the spread of recommended practices and better administrative procedures in practices such as ordering of drugs.

In terms of data entry, when using PDAs, there was a reduction in the number of errors as well as an increase in efficiency. It was also shown that the HCWs preferred to use the stylus based input to enter data where drop down menus were available over keyboard methods [57].

So far the examples given show PDAs being used in situations where resources are plentiful. The next section provides two examples of PDAs being applied in a resource deprived clinics.

5.4 Examples of PDAs Being Deployed in Resource Deprived Clinics

5.4.1 The Ca:sh Project

In Ballabhgarh, northern India, 10 paramedic HCWs have been provided with PDAs to collect patient data and access medical databases. These HCWs operate in a remote and rural area covering a population of 10,000 people.

Like their counterparts in rural Uganda the HCWs of Ballabhgarh have little access to communications technology such as the internet. The PDAs offered the HCWs quick access to patient records. Another benefit offered by the project was that HCWs in the primary healthcare centre were provided with data in an electronic format giving them a greater opportunity to analyse healthcare data.

One of the problems associated with an environment that has no communications technology is the synchronising of data between two locations. The ca:sh project used secure digital (SD) cards to alleviate this problem by physically and securely transporting them between the HCWs in the field and the primary healthcare centre. Not only did this ensure that a backup was made but it also allowed for the synchronisation of data to be made without either party to travel [58].

5.4.2 Satellife

Satellife is a Massachusetts based organisation which used PDAs to collect information in order to determine the efficacy of a measles immunisation campaign in Ghana. They were also used to gather information to conduct an epidemiological survey on malaria in Uganda while in Kenya
they were used by students to collect field survey information. These initiatives were evaluated by bridges.org along with the use of and access to certain medical reference tools and texts. From the evaluation it was concluded that PDAs were a useful technology in the health systems of Ghana, Kenya and Uganda for collecting and disseminating information. In regards to the medical reference material it was concluded that they were of benefit to the physicians and students and they helped improve their provision of healthcare. However, it was also identified that there was a need for more locally relevant content [59]. The next section highlights some considerations that should be taken into account if this content was to be created for a PDA.

5.5 Designing Information Layout on a PDA

Presenting information on a PDA is very different compared to a desktop computer as the screen size is much smaller. Therefore the content that is displayed should be carefully chosen, the amount of graphics and scrolling required should be kept to a minimum [60].

Factors to consider when choosing what content to display should include how regularly the user accesses the data and the urgency of the data. Data that does not fit into either of these categories could be hidden and then viewed when necessary. By keeping the amount of graphics to a minimum, more space is available to display information. An additional benefit is that the download size is reduced.

Finally the level of scrolling required by the user should be minimal as it can be difficult for the user to keep track of their place in the screen [61]. A drill down approach using menu can be used to display information on a number of screens. In cases where it is not possible to divide information by using menus the use of anchors can be applied. However, if the information is transferred to the PDA as a text based document, most of these recommendations can not be implemented. One solution is to write a program using the Java programming language Java 2 Micro Edition (J2ME) which will facilitate the displaying of the content.

5.6 J2ME

The J2ME API is a downsized version of the standard Java 2 platform [62]. An advantage offered by J2ME is that applications programmed in the language can be deployed on a mobile phone as well as a PDA. Considering the high usage of mobile phones in Uganda [63] choosing J2ME as a programming language leaves the possibility for deploying the application on a mobile phone.
There are two main items of influence when dealing with J2ME. These items consist of the Mobile Information Device Profile (MIDP) and the Connected Limited Device Configuration (CLDC).

5.6.1 Mobile Information Device Profile

MIDP is the version of the Java platform developed by the Java Community Process that is based on the CLDC specification and the KVM. MIDP requires a Palm OS of 3.5 or higher.

An MIDP application is known as a MIDlet. MIDlets require that over 128 KB of RAM is available in order to store the implementation. In addition to this 32KB must be available for the Java heap and 8KB of non-volatile memory should the device lose its power source. The non-volatile memory is used to store information that was in use before the device lost its power source. However if the battery is not recharged within a reasonable period of time (2 days) the information could be lost [62].

There are two versions of MIDP although the latest versions are relatively new and as a result documentation to date is sparse. In addition to this, only the most current hardware will support the latest versions of MIDP and CLDC. However, by using the latest versions of MIDP 2.0 and CLDC 1.1, functions that are not available in the older versions such as hyperlinks, floating point numbers and greater screen usage can be taken advantage of.

5.6.2 Connected Limited Device Configuration

CLDC is the building block on which J2ME profiles for small devices are built. These small devices have a limited amount of memory and as a result must use the restricted Java API (Application Programming Interface) that is J2ME. However, as the technology in these small devices improves the J2ME API continues to be expanded to avail of these technologies [62].

The CLDC specifies a minimal set of Java packages and classes by defining the reduced requirements for the language and core libraries while it also defines the reduced functionality Java Virtual Machine (JVM) that can be implemented within the constraints of a small and limited device. Also the CLDC requires that the host platform has a minimum of 32Kb volatile memory to be available for run-time collection which is used to satisfy the dynamic requirements of Java applications such as class loading, allocation of heap space for objects and the stack.
Apart from these memory requirements, the CLDC makes little demands on the hardware and by doing so it maximizes the amount of possible platforms it can be implemented on. The only software assumptions made are that the host device has an OS that can manage and execute the virtual machine (VM). Two virtual machines that conform to CLDC specification include Sun’s KVM and IBM’s J9 VM [62].

Currently there are two CLDC versions available, CLDC 1.0 and 1.1. The older CLDC 1.0 is limited by the absence of support for double and floating-point numbers. In addition to the inability to declare constants, variables and arguments as type float or double, the return of a double or floating point number is not possible. This renders any division of numbers to be very cumbersome. However, due to the advances in hardware technology, the latest CLDC version 1.1 allows for the use of floating point numbers. Support for Java Native Interfaces (JNI) is omitted from both specifications, therefore ruling out the potential to avail of a library or application written in a lower-level programming language [64].

Verification is performed in two stages and ensures that: all the local variables are initialized before use, where appropriate each constructor must begin with an invocation of the super classes constructor and all variables have an appropriate value assigned to them. The first stage is performed after the MIDlet has been compiled and before the MIDlet is installed on the device. This is known as pre-verification and it is the most complex and time-consuming of the two stages. The result is that by not performing pre-verification on the destination device, the amount of processor intensive work along with the amount of memory the destination device requires is reduced. The results given by pre-verification are stored in the class file.

After pre-verification, run-time verification is performed on the destination device. Run-time verification can be done every time the class is loaded or once when the MIDlet is initially installed on the device. In the latter case the results of the pre-verification that were stored in the class file are used.

5.7 Summary

This chapter presented an overview of PDAs. Differences between Palm PDAs and Pocket PCs were discussed and examples where they have been successfully applied in pilot projects were
given. Additionally, important aspects of the programming language J2ME were outlined together with design issues that must be considered when creating an application for a PDA.
6 MARS Application

This chapter looks to build on previous discussions in order to create the MARS application. This is achieved by identifying the user requirements and a guideline architecture for representing the guidelines electronically. Once the user requirements and guideline architecture is established a description of how they are applied to the MARS application is given. In addition, user interaction and some limitations to the application’s creation are explored.

6.1 User Requirements

Referring to the data items listed in Table 4 (page 44) this section identifies the user requirements of MARS. Before doing this, it is important to identify what tasks are carried out by a HCW. It is also essential to clarify which HCWs would be responsible for new tasks that would arise from the introduction of MARS.

Having visited the IDI in Mulago hospital, Kampala, the tasks carried out by HCWs were identified and these are illustrated in Figure 10. Certain tasks, such as recording the patients’ details and updating them were performed by a nurse. Other tasks including administering and monitoring a patient on ART were carried out by the doctor. While this is the normal practice, it is possible that in a rural clinic all of these tasks would be performed by one HCW, who may not be a doctor.

With the introduction of MARS into the UHS it is proposed that the creation, assessment and updating of CPGs would be carried out by an expert in HIV/AIDS at the National Level of the UHS. HCWs at lower levels would not be expected to carry out these tasks. Other potential tasks that may be carried out by a HCW in the event of MARS being integrated into their work practice are outlined in Figure 10. These include updating the patient record by syncing the data on the PDA with a patient database.

Figure 10 also illustrates the need to apply ICD codes to infections that have been identified for a particular patient. In Uganda ICD codes are applied by a recorder after a diagnosis has been made and all the notes have been taken on the patients’ current visit. However, this process is not always implemented as recorders are not present at all levels [18].
Tasks that are illustrated in Figure 10 which are relevant to MARS translate into the following user requirements:

a) MARS should supply a HCW with a recommended regimen for treating a patient infected with HIV/AIDS. This regimen should be based on data entered into an EPR and the current guidelines for treating HIV/AIDS in Uganda. By giving the HCW support in administering ARVs it is hoped that the likelihood of a patient being prescribed harmful regimens is reduced. Another potential benefit could be a reduction in ARV resistant strains of the virus due to the patients being placed on a more synergistic regimen.

b) MARS should apply ICD codes to the diseases which a patient has been diagnosed of. This would allow for an easier analysis of epidemiology while it would also provide a standard method for naming diseases in a clinical guideline.

---

1 Three HCWs (Actors) were used in this use case diagram instead of one for readability purposes.
c) MARS should be able to review patients currently on ART and issue warnings to a HCW should a patient be showing signs of treatment failure.

d) It should be possible for MARS to create, update, view and alter an EPR which is stored on a central server.

e) At each patient visit MARS should issue a reminder to the HCW if a patient is to go for tests before their next visit.

The next section begins with a description of the methodology that was applied in order to provide a HCW with a recommended ARV regimen (user requirement - a). It is followed by the selection of a means for representing the guidelines in electronic format. Finally decision criteria that was extracted from the written guidelines and used to create the rules is presented.

### 6.2 Provision of ARV Decision Support

MARS provides restricted decision support for the administering of ARVs by applying a similar methodology to one which is used by the Bloodlink-Restricted decision support system. Bloodlink-Restricted provides general practitioners (GP) in selected clinics in Holland with a decision support system for ordering blood tests. It presents a GP with fifteen tests which cover the majority of clinical situations. Once they have selected and placed the orders, they are recorded in the EPR [65].

In the case of the MARS application a number of infections that are common in PLWA will be presented. The HCW will also be given a list of common medicines such as Rifampicin which is used to treat tuberculosis. Using these lists the HCW will be able to ‘tick off’ which infections the patient has and the medications that they are currently taking or have recently taken. By applying the data entered by the HCW to a set of rules, MARS will offer a recommended regimen to the HCW which they can either accept or reject.

#### 6.2.1 Guideline Architecture

Having reviewed both rule based and process oriented guideline architectures, it is apparent that ECA rules would be more suited to the provision of a decision support application for the administration of ARV drugs.

A process oriented approach is more appropriate for representing a guideline that unfolds over time [51]. When providing a HCW with decision support for administering ARVs it is not
necessary to monitor the guideline over time, as it should not change provided the regimen is suitable for the patient. Process oriented guidelines also take into account the state of the patient. In sub-Saharan Africa patients frequently miss the initial diagnosis of HIV and consequently the vast majority of cases will be at the final stage of the disease. The result is that only one patient state will be taken into account and therefore the need for recording patient states’ in the guidelines is reduced.

When a patient is deemed ready to start ART, the process of deciding what regimen to place them on is based on a number of rules. For example a patient who is pregnant can not be placed on a regimen containing the NNRTI, EFV as it has a teratogenic effect in primates. By using a rule based architecture such as Arden Syntax or PLAN, it is possible to encapsulate these rules electronically.

6.2.2 Choosing an ECA architecture

Table 6 lists decision criteria considered when choosing Arden Syntax over PLAN. A notable advantage offered by Arden Syntax is that it is an officially recognised standard for representing guidelines. As a result many guidelines for other conditions have been created using Arden Syntax, some of which consist of HIV/AIDS OIs. Therefore it could be possible to provide greater decision support to the HCW by availing of these existing guidelines. Another advantage of Arden Syntax is the amount of literature that is available on the architecture. This is further enhanced by the existence of software which can validate the syntax of a guideline.

<table>
<thead>
<tr>
<th></th>
<th>Arden Syntax</th>
<th>PLAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static Rules</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Dynamic Rules</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Patient State</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Patient Specific</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Time Functions</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Shareable</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Nesting</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Validation</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Literature</td>
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<td>NO</td>
</tr>
<tr>
<td>Standard</td>
<td>YES</td>
<td>NO</td>
</tr>
</tbody>
</table>

Table 6: PLAN vs Arden Syntax

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Anything which produces non-heritable birth defects is said to be teratogenic.
6.2.3 Creating the ECA Rules

Once it was decided to represent the CPGs using Arden Syntax, a manual process of extracting rules from the written guidelines and converting them into Arden Syntax was conducted. The major items influencing the rules that were taken from the written guidelines are listed in Table 7. Figure 11 shows a guideline for the provision of firstline ART which was created following this process.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 Count</td>
<td>Required for most cases before ART has commenced. HIV+ patients taken every 6 – 12 months</td>
</tr>
<tr>
<td>TB (A16.2)</td>
<td>In most cases patients who have TB don’t start ART until it has been treated</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>NVP or a selection of PIs cannot be taken with this drug</td>
</tr>
<tr>
<td>Pregnant or potential</td>
<td>Cannot take EFV</td>
</tr>
<tr>
<td>Anaemic (D60)</td>
<td>Patient cannot start therapy.</td>
</tr>
<tr>
<td>Taking ARVs</td>
<td>Stopped taking them? How long ago? What was taken? Still taking them what ones?</td>
</tr>
<tr>
<td>Psychiatric Illnesses</td>
<td>Taking EFV should be avoided</td>
</tr>
<tr>
<td>Weight</td>
<td>Should be taken every visit</td>
</tr>
<tr>
<td>Age</td>
<td>For paediatric regimens</td>
</tr>
<tr>
<td>WHO Stage of illness</td>
<td>If some diseases are presented a CD4 count may not be necessary</td>
</tr>
</tbody>
</table>

Table 7: Factors of influence when prescribing a regimen for ART.
firstLine := event("Choose the firstline regimen for the patient");

if
  last_HB < 8
then
    alert_text := "Anaemic";
    conclude true;
elseif
    AIDSDefining = "A16.2"
then
    alert_text := "Patient has TB. Refer to Coinfections";
    conclude true;
elseif
    last_CD4 < 200 and pregnant = false and historyPsy = false
then
    alert_text := "Recommend: AZT/3TC/NVP or d4T/3TC/NVP or AZT/3TC/EFV or d4T/3TC/EFV";
    conclude true;
elseif
    last_CD4 < 200 and pregnant = true and historyPsy = false
then
    alert_text := "Recommend: AZT/3TC/NVP or d4T/3TC/NVP";
    conclude true;
elseif
    last_CD4 < 200 and pregnant = false and historyPsy = true
then
    alert_text := "Recommend: AZT/3TC/NVP or d4T/3TC/NVP";
    conclude true;
elseif
    last_CD4 < 200 and pregnant = true and historyPsy = true
then
    alert_text := "Recommend: AZT/3TC/NVP or d4T/3TC/NVP";
    conclude true;
endif;

action:
    write alert_text;

Figure 11: Rules for firstline therapy

6.3 Applying the ECA Rules to MARS

After the rules had been converted into Arden Syntax they were embedded into the MARS application as Java if-then-else statements following a manual conversion process. Given more development time, this practice would be eliminated by adding additional functionality to MARS which would allow for the interpretation of rules in Arden Syntax format.

In order for MARS to produce a recommended ARV regimen, the ECA rules require that patient data be input in a structured manner. The next three sections describe the processes of entering patient data, handling the data once it has been entered, and assessing the data to produce a regimen.
6.3.1 Entering Patient Data

A HCW is initially presented with a form (Figure 12) which allows for a patient’s clinical details to be input. How this data is entered depends on the device on which MARS resides. For example should the HCW be using a mobile phone, data would be entered via the phones’ keypad. Alternatively if MARS is hosted on a PDA the data could be input using a stylus and the onscreen keyboard or Graffiti. It is also possible to use peripherals such as an attachable keyboard instead of the stylus.

Pop-up menus have been used to reduce the amount of text that is input manually. This allows for an easier interpretation of the data while permitting clutter to be kept to a minimum.

![Figure 12: Patient Details Screen](image)

![Figure 13: Recommended Regimen display to the user](image)

![Figure 14: Entering Diagnoses into MARS](image)
6.3.2 Handling Data Input

Once the HCW has completed entering patient data and selected ‘Ok’ a Patient class is instantiated by the MIDlet MARS. The class Patient as illustrated in Figure 16 contains a number of fields and methods which allow for the storing and manipulation the patient’s vital statistics. Patient is then passed into the class Evaluator where it is assessed (Section 6.3.3 provides a more detailed account of this assessment). Following Evaluator’s assessment a string containing a recommended regimen for the patient is returned to MARS. This string is displayed to the user on a form (Figure 13) while it also stored in the Patient class as a record of the patient’s ARV regimen. Finally the patient’s details are written to an SD card in XML format. In cases where a network connection is available this data could be sent to a patient database.

<table>
<thead>
<tr>
<th>Disease.xml</th>
<th>Drug.xml</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;disease&gt;</td>
<td>&lt;drug&gt;</td>
</tr>
<tr>
<td>&lt;code&gt;123.39&lt;/code&gt;</td>
<td>&lt;generic&gt;Lamivudine&lt;/generic&gt;</td>
</tr>
<tr>
<td>&lt;name&gt;Prolonged Fever (&gt;1 months)&lt;/name&gt;</td>
<td>&lt;brand&gt;Epivir&lt;/brand&gt;</td>
</tr>
<tr>
<td>&lt;stage&gt;4&lt;/stage&gt;</td>
<td>&lt;code&gt;3TC&lt;/code&gt;</td>
</tr>
<tr>
<td>&lt;/disease&gt;</td>
<td>&lt;/drug&gt;</td>
</tr>
<tr>
<td>&lt;disease&gt;</td>
<td>&lt;drug&gt;</td>
</tr>
<tr>
<td>&lt;code&gt;123.40&lt;/code&gt;</td>
<td>&lt;generic&gt;zidovudine&lt;/generic&gt;</td>
</tr>
<tr>
<td>&lt;name&gt;Extrapulmonary Tuberculosis&lt;/name&gt;</td>
<td>&lt;brand&gt;retrovir&lt;/brand&gt;</td>
</tr>
<tr>
<td>&lt;stage&gt;4&lt;/stage&gt;</td>
<td>&lt;code&gt;AZT&lt;/code&gt;</td>
</tr>
<tr>
<td>&lt;/disease&gt;</td>
<td>&lt;/drug&gt;</td>
</tr>
</tbody>
</table>

Table 8: Table showing the structure of the files Disease.xml and Drug.xml

When a patient’s known diagnoses are being recorded (Figure 14) each diagnosis that is checked on the form is placed into a dynamic array known as a vector. This vector of diseases is then compared with an XML file called diseases (Table 8). Should a disease in the vector match a disease name in the XML file an instance of the disease class is recorded in the Patient class. This includes the disease’s name, ICD code and WHO stage number. Figure 15 illustrates this process in a dataflow diagram. The entire process is identical for the recording of the patients’ medication history where the drugs entered in the form are compared with an XML called drugs. Any matches are recorded in Patient as a Drug class which holds the brand name of the drug, the generic name and the code.
Figure 15: Dataflow diagram illustrating the assignment of ICD codes to a disease
Figure 16: Class Diagram of MARS Evaluating Patient Data
6.3.3 Producing a Recommended Regimen

As was mentioned in the previous section the *Evaluator* class is responsible for assessing a patient’s details and using them to generate a recommended regimen for a patient. When an Evaluator class is instantiated a *Patient* object is passed into it as an attribute. Methods belonging to *Patient* are then used to extract data from the object which are in turn assessed by the *Evaluator* methods. The methods in *Evaluator* can be divided into two sets of groups – one group produces a recommended regimen and the other generates a dosage rate for a particular drug. In total nine methods relating to nine different drugs exist. The drugs accounted for include ddI, d4T, 3TC, EFV, NVP, AZT, NFV, LPV and SQV. Additionally five methods exist which produce a recommended regimen and together they encapsulate the Ugandan guidelines for providing ART.

Figure 17 presents a high level illustration of the entire process as described in sections 6.3.1 to 6.3.3. The following section documents some of the limitations that were encountered during the implementation of MARS.
6.4 Limitations of Programming on a Mobile Device

When developing an application for a mobile device there are some notable limitations in comparison to developing an application for a desktop computer. Firstly the memory available for storing and running an application is considerably less on a mobile device. Another limitation is the smaller processing speed. As previously mentioned MARS compares a vector of disease names with disease names in an XML file. In order for this task to be completed an XML parser is required. Traditional XML parsers require a large amount of runtime memory and feature hefty amounts of code. The result is that they are unsuitable for constrained devices [66] and parsers specifically designed for MIDP had to be created. kXML is one of these parsers and was successfully deployed in MARS.
Another tool used in MARS which helped to reduce the size of the application was the obfuscator - Retroguard. An obfuscator reduces the size of the application by removing any unused classes, methods or variables. It also renames classes, packages, methods and variables with smaller names. Obfuscators also add code to classfiles which, can confuse decompilers.

6.5 Summary

This chapter has given the reader an account of the MARS application. In doing so, user requirements were identified along with a guideline architecture – Arden Syntax. Reasons for choosing Arden Syntax as a method for electronically structuring the Ugandan ART guidelines were also provided. In addition, the criterion that was considered when deciding upon a recommended regimen was presented. Finally some limitations to the application’s creation were outlined. The next chapter describes the methodology and results of evaluations of MARS 1.0 and MARS 2.0.
7 Evaluation

During the course of this evaluation two versions of the MARS application were created. This chapter presents the methodology and results of limited evaluations that were conducted for each version. Comparisons between the two versions are also given.

7.1 Evaluation of MARS 1.0

The test group consisted of 10 African doctors with each having 3 years or more post graduate experience and two having experience in treating HIV/AIDS. They were given 3 sample cases to read and answer questions on with a time period of 5 minutes being allotted to each case. The class was divided randomly into 3 groups. Group A was the control group with 3 people, one being experienced in treating HIV/AIDS, Group B which comprised of 4 people and one of these had experience in treating HIV/AIDS. Group B used a hardcopy of the guidelines. Group C which was formed from the remaining 3 members of the class used the electronic version of the guidelines. Only one member of the group had experience using a PDA which was a Pocket PC.

Groups B and C were given questionnaires (Appendix 3 – MARS 1.0 Questionnaire) on the methods of representation of the guidelines. Two members of group C agreed and one strongly agreed that the application was easy to use and that the information was easy to find. All strongly felt that information in the application was detailed enough to help them make an informed decision and that menus were well laid out. 2 agreed that the application performed efficiently with the other strongly agreeing. Finally, 2 members of the group strongly agreed and one agreed that the information was displayed in a clear and legible manner. The majority agreed that the screen layout was intuitive.

Group B had a mixed response to the paper version of the guidelines. 2 members of the group disagreed that the guidelines were easy to use while one agreed and the other strongly agreed that the guidelines were easy to use. Regarding the lay out the information 2 strongly disagreed and one disagreed that the information was easy to find while the remaining member agreed with the statement. Interestingly 2 disagreed that the information contained in the guidelines helped them to make an informed decision while 2 agreed with the statement. Compare this to Group C who...
all strongly agreed to the statement even though the information they were provided with was the same.

Table 9 shows the results of the test. As can be seen from the results, group A failed to perform as well as groups B or C who had some form of guidelines. Of the 2 groups with guidelines C performed marginally better overall. In case 2 group C only answer 3 out of the five questions. Interestingly, despite the fact that groups A and B contained a doctor who had experience in the provision of ART, group C outperformed them by getting 10 of the 13 questions right.

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grp A</td>
<td>2/3</td>
<td>0/5</td>
<td>2/5</td>
<td>4/13</td>
</tr>
<tr>
<td>Grp B</td>
<td>2/3</td>
<td>5/5</td>
<td>2/5</td>
<td>9/13</td>
</tr>
<tr>
<td>Grp C</td>
<td>3/3</td>
<td>3/5</td>
<td>4/5</td>
<td>10/13</td>
</tr>
</tbody>
</table>

Table 9: Results of Evaluation of MARS 1.0

7.2 Evaluation of MARS 2.0

A second evaluation which assessed the performance of MARS 2.0 in comparison with the paper based guidelines, on terms of usability and efficiency was also conducted. Two written cases accompanied with a questionnaire (Appendix 4 – MARS 2.0 Questionnaire) and extracts from the Ugandan Guidelines for ART were given to a group of seven HCWs. The group consisted of 2 nurses trained in midwifery, a theatre nurse, 2 radiotherapists and a retired nurse.

On each occasion the HCW was allocated time to familiarise themselves with the written guidelines before reading any of the cases. A small demonstration of MARS 2.0 was also provided. Once they were familiar with the guidelines, one of the two cases was given to the HCW and the time was noted. Using the written guidelines for the first case the HCW was asked to recommend an ART regimen for the case. They were also required to recommend a dosage rate for each ARV of the regimen. Once a recommendation and the doses for each ARV had been made the time was noted. At this point a second case together with MARS 2.0 was given to the HCW while the written guidelines were taken back from them. The time was also noted. Again the HCW was required to recommend an ART regimen and doses for each drug using MARS 2.0. After a decision had been made on which regimen to use and the doses to give the time was noted again. The HCW was then required to give their opinion on a statement which compared the
written guidelines with MARS. Finally they were asked note any comments they had on the
application. The recommendations they had made were then compared with recommendations
provided by a pharmacologist from SJH.

When using the written guidelines all seven HCWs provided the correct regimen. One of the
seven prescribed the wrong dose for the drug EFV and the average time taken to provide a
recommendation and doses was 452.5 seconds. When MARS was used for the second case, six of
the seven HCWs provided the correct regimen. The one incorrect regimen was prescribed as
result of the HCW failing to enter a drug which the patient was taking for TB. Of the six correct
cases all of the doses prescribed were correct. The average time taken to prescribe a regimen and
dose using MARS was 223.3 seconds.

All the participants strongly agreed that MARS was easier to use than the paper based guidelines.
One participant in the study commented that the application was less demanding and that it
simplified a complicated process. Other suggestions were made on how to improve the layout of
the content on the screen to make it less ambiguous while another participant suggested that the
field’s weight, age and height be checked for blank data entries before the data is submitted for
evaluation.

7.3 Summary

The results from the evaluation of MARS 1.0 show that there is little difference between
transferring written guidelines directly into an application for a PDA. Although it is more
culturally acceptable for a HCW to use a PDA such a solution may not be cost effective in health
systems which are struggling to provide ARVs for HIV positive people as it would not be
maximising the potential of the PDA.

The evaluation of MARS 2.0 demonstrated that by encapsulating the guidelines in an ECA rule
based application it is possible for a HCW to be presented with an accurate drug regimen and its
associated doses provided the correct information is supplied. It also showed that the amount of
time spent reviewing the guidelines is more than halved as the application evaluates the data for
the HCW. In comparison to the first version, MARS 2.0 takes full advantage of the processing
ability of the PDA. MARS 2.0 evaluates the patient data to produce an ARV regimen unlike
MARS 1.0 which requires that the HCW locate the information they require. It also facilitates the
collection of epidemiology statistics in the form of ICD codes.
8 Discussion

8.1 Future Work

In order for MARS to be implemented in a clinic, a comprehensive EPR is necessary. At present all patient data is recorded in paper format in rural clinics. Therefore all the information required by the guidelines has to be manually entered into MARS for a recommendation to be made. However, should the information be already stored in an EPR, the application could retrieve data regarding the patients’ medical history, thus reducing the amount of data that has to be entered manually. Also by having the patients’ record stored electronically it is easier to incorporate the CPGs into clinics’ work practices by providing a HCW with reminders and warnings. For example, it would be easier to monitor the patients progress when prescribed ART, as once they start to show signs of treatment failure, warnings coupled with alternative drug regimens could be displayed to the HCW.

Having reviewed the structure of the UHS it is clear that a centralised approach to storing patient information should be applied. Such an approach would ensure that remote clinics starved of resources such as electricity would not be responsible for the storing of data. This responsibility would fall on the more adequately equipped higher level clinics thus leaving the lower level clinics accountable for the storing and forwarding clinical information to them when a network connection is available. Additionally, it would also be possible for clinical information such as recommended practices to be passed from the higher level clinics down to the lower level clinics via this structure.

The method for transferring data between clinics would only need to be asynchronous, as the nature of the disease and the current methods for treating it do not require instant feedback. Also the current electric infrastructure does not provide a guaranteed source of electricity and therefore network downtime could be frequent. Possible methods for transferring data which have been identified include using an SD card to physically transport data and satellite communications, each having their own advantages and disadvantages.

In circumstances where cost and sustainability is an issue, SD cards could be incorporated in the work practice of the clinics. In this situation it is suggested that the patient could carry the SD card with them when they are attending a higher level clinic for VCT or tests such as CD4 counts.
which are taken every six months. On arrival at the higher level clinic the patient could present
the SD card which would hold all of their recent clinical data. This clinical data could then be
uploaded and stored in the higher level clinic. In cases where the patient is attending the higher
level clinic for tests the results could be recorded both on the SD card and on the local database.
Where the test results are not immediately available the SD card could be posted back to the
lower level clinic with the results stored on the SD card.

Alternatively, a satellite would offer a more reliable method of transferring data between clinics
as the likelihood of the clinical data being lost would be considerably less. Also, the frequency in
which clinical data could be exchanged would be far greater. Another potential benefit is that a
satellite could be used to provide the community with internet access and as a result educational
establishments would have greater access to knowledge resources. These methods however would
be more costly and therefore less sustainable.

Regarding the MARS application, numerous additional functions could be added after a more
comprehensive evaluation is conducted. One possible function would allow for a HCW to notify
an expert, who is responsible for the construction of the guidelines, with information regarding a
case that has not been accounted for. This could be achieved by providing the HCW with an
option to text or email the expert the details of the case. The expert would then be able to respond
to the message and also make the necessary adjustments to the rule base.

An additional feature that could be added to MARS would enable a HCW to enter diseases not
listed on the data entry form. The entry could then be recorded in the EPR, as well as in the log
file which would be sent to the designers of the CPGs, in a manner similar to the one described in
the previous paragraph.

Information regarding the ARVs that are being prescribed to the patient could also be provided to
the HCW. This would include details such as the possible adverse effects of the drug, any storage
requirements and the expected price.

MARS should also include rules that provide a HCW with decision support for prescribing ARVs
to women who are about to give birth. This is essential due to the number of children being born
with HIV because of MTCT, which is in the majority of cases preventable provided the mother is
given the appropriate treatment. Additional rules could also be included on the provision of post
exposure prophylaxis (PEP) which is administered to HCWs following an occupational exposure to potentially infectious material.

8.2 Conclusions

This dissertation examined the use of ICD codes as a means to link patient data with CPGs for treating HIV/AIDS. The codes proved successful when applied for this purpose, although the extent to which they were tested was limited. By using the codes a standard method of naming a disease in the CPG can be used, eliminating the problem caused by synonyms. For example extra pulmonary can also be referred to as disseminated tuberculosis. The result is that CPGs which are shared amongst institutions do not have to be altered in order to conform to a particular institutions naming scheme. Another benefit of applying ICD codes to the patient data arises from their storage in the EPR instead of text, thus allowing for easier analysis of the epidemiology of a clinic.

The potential for using mobile technology in resource starved areas was also investigated in this dissertation. It was shown that PDAs have been successfully applied in pilot projects in Uganda, Ghana, Kenya and India. As a result a PDA was chosen to host the Ugandan CPGs for HIV/AIDS.

By choosing to use a PDA several options of design were removed. One such option was the capturing of the CPGs using a process oriented approach similar to one applied by MediLink. This would not have been feasible as the rules created from the UML diagrams would be too large for a PDA to process. As a result the CPGs were stored in the form of ECA rules which required less processing as they were created manually. Another restriction related to the choice of programming language. J2ME, a cut down version of Java created for mobile devices such as PDAs and mobile phones had to be used in order to comply with the hardware requirements. Despite these restrictions, a PDA was considered more suitable than a laptop or PC because of the lack of a guaranteed power supply in parts of Uganda. Additionally PDAs are cheaper to buy than a PC or a laptop and they are easier to use.

After evaluating MARS it was clear from the response of participants that the application was easier to use than the paper based guidelines. However, with one evaluation producing an incorrect regimen as a result of the participant failing to enter all the vital information, the need for accurate data entry was highlighted. This may be less of a problem in certain cases where
MARS is linked to a comprehensive EPR, as the amount of data required to be entered manually would be reduced thus reducing the likelihood of erroneous recommendations.
9 Appendices

Appendix 1 – Example of Arden Syntax

maintenance:

title: Diagnosis of Pregnancy to Trigger Health Maintenance Rules;
filename: Pregnancy_Diagnosis;
version: 1.13;
itstitution: Columbia-Presbyterian Medical Center;
author: Eric Sherman (sherman@cucis.cis.columbia.edu);
specialist: ;;
date: 1994-10-13;
validation: testing;

library:

purpose: ;;
explanation: ;;
keywords: ;;
citations: ;;

knowledge:

type: data-driven;
data:

preg_test := event {'32506','1751'; '32506','28177';
'32506','35858'; '32506','36137';
'32506','36340'};

Bhcg := read last
{'evoking','dam"PDQRES2"';
'1751','28177','35858','36137','36340'};

pospatterns := ("POSITIVE","POS",">");  
negpatterns := ("NEGATIVE","NEG","<");

last_delivery := read (  
{"dam"="GYDAPMP";"HDIAGNOS";"HDIAGCOD")
where they occurred within the past 1 month);

last_alert := read last (  
{"dam"="PDQDEC1"; "mlm Pregnancy_Diagnosis"; '32758'})
where it occurred within the past 9 months);

submlm1 := mlm 'Prenatal_HepBsAg';
submlm2 := mlm 'Prenatal_GC_Culture';
submlm3 := mlm 'Prenatal_Chlamydia';
submlm4 := mlm 'Prenatal_AFP';
submlm5 := mlm 'Prenatal_Anemia';
submlm6 := mlm 'Prenatal_Syphilis';

/ * E-mail address*/
email_dest := destination
    {'email', 'name'="sherman@cucis.cis.columbia.edu"};

;;
evoke: 1 minute after time of preg_test;;
logic:
    if Bhcg is null then
        conclude false;
    endif;

    if Bhcg is number then
        if Bhcg < 2 then
            conclude false;
        endif;
        else
            if any negpatterns are in Bhcg then
                conclude false;
            elseif any pospatterns are in Bhcg then
                ;
            else
                conclude false;
            endif;
        endif;
    endif;

    if last_alert is null then
        ;
    else
        if time of last_delivery is null or
        time of last_delivery is after time of last_alert then
            ;
        else
            conclude false;
        endif;
    endif;
/*delay 1 minute;*/

/* If there is a history of abortion */
/*    - spontaneous or scheduled - */
/* or delivery since the last positive B-HCG */
/* then the patient is not longer pregnant */
/* These procedures are discovered using ICD9-CM codes. */
if any (diag_type = "85.42" or
        diag_type = "85.44" or
        diag_type = "85.46" or
        diag_type = "85.48") then
    conclude false;
endif;

if time of last_alert is after 1 minute before now then
    conclude false;
endif;
if time of last_delivery is after 1 minute before now then
    conclude false;
endif;

conclude true;
action:
    write "the B-HCG value is " || Bhcg at email_dest;
    call submlm1;
    call submlm2;
    call submlm3;
    call submlm4 delay 2 minutes;
    call submlm5;
    call submlm6;

end:
Appendix 2 – WHO Stages

Clinical stage I
1. Asymptomatic
2. Persistent generalized lymphadenopathy

Performance scale 1: asymptomatic, normal activity

Clinical stage II
3. Weight loss, <10% of body weight
4. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
5. Herpes zoster within the last five years
6. Recurrent upper respiratory tract infections (i.e. bacterial sinusitis)
   And/or performance scale 2: symptomatic, normal activity

Clinical stage III
7. Weight loss, >10% of body weight
8. Unexplained chronic diarrhoea, >1 month
9. Unexplained prolonged fever (intermittent or constant), >1 month
10. Oral candidiasis (thrush)
11. Oral hairy leukoplakia
12. Pulmonary tuberculosis within the past year
13. Severe bacterial infections (i.e. pneumonia, pyomyositis)
   And/or performance scale 3: bedridden <50% of the day during the last month

Clinical stage IV
14. HIV wasting syndrome, as defined by the Centers for Disease Control and Prevention
15. Pneumocystis carinii pneumonia
16. Toxoplasmosis of the brain
17. Cryptosporidiosis with diarrhoea >1 month
18. Cryptococcosis, extrapulmonary
19. Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes
20. Herpes simplex virus infection, mucocutaneous >1 month, or visceral any duration
21. Progressive multifocal leukoencephalopathy
22. Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis)
23. Candidiasis of the oesophagus, trachea, bronchi or lungs
24. Atypical mycobacteriosis, disseminated
25. Non-typhoid Salmonella septicaemia
26. Extrapulmonary tuberculosis
27. Lymphoma
28. Kaposi’s sarcoma
29. HIV encephalopathy, as defined by the Centers for Disease Control and Prevention.
And/or performance scale 4: bedridden >50% of the day during the last month
Appendix 3 – MARS 1.0 Questionnaire

**Questionnaire**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you used a Palm PDA before?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Have you used a Pocket PC before?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Do you own a Palm PDA or a Pocket PC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. If you own a PDA what make and Model is it?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For each of the following statements (a)-(e) shown below, circle the number that is closest to your own view, where 4 means that you strongly agree with the statement and 1 means that you strongly disagree.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.</td>
<td>The application was easy to use.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>The information I needed was easy to find.</td>
<td></td>
<td></td>
<td></td>
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<td>7.</td>
<td>The content contained enough detail to help me make an informed decision.</td>
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<td>8.</td>
<td>The menus gave a strong indication to the information that followed.</td>
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<td>9.</td>
<td>The application performed without any long delays.</td>
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<td>10.</td>
<td>The information was laid out in a clear and legible manner.</td>
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<td>11.</td>
<td>The screen layout was intuitive.</td>
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<td>12. Please note below any other comments that you have on the current application.</td>
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<td>13. Please note below any suggestions you may have that may improve the application</td>
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Appendix 4 – MARS 2.0 Questionnaire

Mobile AntiRetroviral Support (MARS) Evaluation

Instructions
a) You will be given 10 minutes to read extracts from the current Ugandan guidelines for Antiretroviral Therapy.

b) After reading the guidelines two cases will be given to you to read.

c) For the first case you will use the written guidelines to recommend a drug regimen and doses for each drug.

d) For the second case you will be provided with a PDA to aid you in the prescribing of a drug regimen and the doses for each drug.

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<tr>
<th>Job Title:</th>
<th>Years Experience:</th>
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Have you ever prescribed or administered ARVs to a HIV positive patient? Yes / No

Case One
A 23 year old man comes to the clinic with a cough of six weeks duration. At present he weighs 56 kg but has lost 11 kg over the last month. Diagnosed with pulmonary tuberculosis, he is taking Rifampicin. The tuberculosis clinic also performed a CD4 test and his CD4 count is 209. In addition he has suffered from oral candidiasis within the last year.

1) What ARV regimen would you prescribe to this patient?

2) What dose would you recommend for each ARV?

Case Two
An 18 year old pregnant woman presents with lymphadenopathy and pulmonary tuberculosis for which she is taking Rifampicin. She is confirmed HIV positive with a CD4 count of 80 and a Hb level of 11 g/dL and her weight is 55 kg.

1) What ARV regimen would you prescribe to this patient?
2) What dose would you recommend for each ARV?

Using a scale of 1 – 4 where 1 indicates that you strongly disagree and 4 indicates that you strongly agree please answer the following questions by circling the appropriate number.

The application was easier to use than the paper based guidelines:

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<td>4</td>
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<tr>
<th>Time taken:</th>
<th>Case 1:</th>
<th>Case 2:</th>
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<tr>
<td>Completed all cases: Yes or No</td>
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General comments on the application:

If you got either case wrong do you know why? Yes or No

If you are aware of why you got a wrong answer can you provide the reason.
10 References


[18] Woods, G., Personal Interview with Fred Kakaire, CEO Ugandan Healthnet, 29th October 2004


[29] King, R.W., Potency of Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs) Used in Combination with Other Human Immunodeficiency Virus NNRTIs, NRTIs, or Protease Inhibitors, Antimicrobial Agents and Chemotherapy, 2002, p 1641.


