The School of Pharmacy
University of London

Cardiovascular Drug Utilisation in Jordanian Hospitals

Thesis submitted in accordance with the requirements of the University of London for the degree of Doctor of Philosophy by

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2006
Cardiovascular Drug Utilisation in Jordanian Hospitals

Plagiarism Statement in Thesis

This thesis describes research conducted in the School of Pharmacy, University of London between 2000 and 2006 under the supervision of Professor Soraya Dhillon and Professor Felicity Smith. I certify that the research described is original and that any parts of the work that have been conducted by collaboration are clearly indicated. I also certify that I have written all the text herein and have clearly indicated by suitable citation any part of this dissertation that has already appeared in publication.

Signature

Date

October 2006
Acknowledgment

To God, thank you for this journey and granting me the chance to learn and develop...

To the people I cherish most:
My parents; Abdel Bari and Safa...
My husband; Abulwafa...
My family; Abeer, Mohammed, Basil, Khalid, and Jamal...
Thank you for your love, encouragement and patience throughout my PhD..

Special thanks to my friends Reem and Hind Abunahl for making London feel like home..

I would also like to thank my supervisors Professor Soraya Dhillon and Professor Felicity Smith for their guidance and support in the supervision of this work. Thanks also to Dr. Abdullah Al-Khawad for his considerable support during the first year of the project, Dr. Eyas Al-Moussa, Dr. Nazih Kadri, Dr. Ahmad Hassonah, and Dr. Hani Al-Khateeb for their distinctive contribution to this project. I hope this is the beginning of more collaboration in the future..
Abstract

The overall aim of this project is to evaluate cardiovascular drug utilisation in Jordanian hospitals, to identify gaps in practice and to propose areas for pharmacists’ contribution in patient care. In order to achieve this aim, several objectives had to be fulfilled. These comprised:

I: Description of the health conditions and health care system in Jordan. This involved conducting a literature review and in-depth interviews with key health care professionals in Jordan. The epidemiological profile and primary health problems in the Jordanian population were identified. Furthermore, the health care sectors, services, facilities, manpower and performance were presented. In particular, the hospital systems were explored in terms of the factors which influence medical practice, drug use and availability, patient care, and role of medical team members, with focus on the role of hospital pharmacists. Additionally, the pioneer experience of clinical pharmacy practice at the army hospitals was described.

II: Description of drug use practices in cardiac diseases at Jordanian hospitals. Patient records were prospectively reviewed for 98 patients over a five-day period at three hospitals. The prescribing patterns, therapy monitoring and follow up of cardiac patients were described.

III: Development of a tool for the assessment of cardiovascular drug utilisation. Four templates of explicit drug use evaluation criteria were developed for the diseases: stable angina, unstable angina, myocardial infarction and heart failure. The templates were based on international cardiology guidelines, and adapted by a panel of senior cardiologists in Jordan to assure their applicability at local settings. The methods and outcome from developing local guidelines were discussed.

IV: Evaluation of cardiovascular drug use in coronary heart diseases and heart failure. The ongoing prescribing and monitoring practices were assessed against the above developed templates in 61 patients. Gaps in practice were identified.

The project concludes with recommendations on how to optimise drug use and the areas to which pharmacists can contribute to patient care at secondary level.
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<td>ACC</td>
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<td>AHA</td>
<td>American Heart Association.</td>
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<td>ARBs</td>
<td>Angiotensin Receptor Blockers.</td>
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<td>BNF</td>
<td>British National Formulary.</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure.</td>
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<td>CCB</td>
<td>Calcium Channel Blockers.</td>
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<td>DOS</td>
<td>Department of Statistics.</td>
</tr>
<tr>
<td>DUE</td>
<td>Drug Use Evaluation.</td>
</tr>
<tr>
<td>EMRO</td>
<td>Eastern Mediterranean Regional Office of WHO.</td>
</tr>
<tr>
<td>ESC</td>
<td>The European Society of Cardiology.</td>
</tr>
<tr>
<td>GTN</td>
<td>Glyceryl Trinitrate.</td>
</tr>
<tr>
<td>HC</td>
<td>Hypercholesterolaemia.</td>
</tr>
<tr>
<td>HCC</td>
<td>Health Care Centre.</td>
</tr>
<tr>
<td>HCPs</td>
<td>Health Care Professionals.</td>
</tr>
<tr>
<td>HDL</td>
<td>High Density Lipoprotein.</td>
</tr>
<tr>
<td>HF</td>
<td>Heart Failure.</td>
</tr>
<tr>
<td>HTG</td>
<td>Hypertriglyceridaemia.</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension.</td>
</tr>
<tr>
<td>IGT</td>
<td>Impaired Glucose Tolerance.</td>
</tr>
<tr>
<td>ISDN</td>
<td>Isosorbide Dinitrate.</td>
</tr>
<tr>
<td>IHD</td>
<td>Ischemic Heart Diseases.</td>
</tr>
<tr>
<td>JD</td>
<td>Jordanian Dinars.</td>
</tr>
<tr>
<td>JFDA</td>
<td>Jordan Food and Drug Administration.</td>
</tr>
<tr>
<td>JUH</td>
<td>Jordan University Hospital.</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>JVP</td>
<td>Jugular Venous Pressure.</td>
</tr>
<tr>
<td>LDL</td>
<td>Low Density Lipoprotein.</td>
</tr>
<tr>
<td>LOS</td>
<td>Length of Stay.</td>
</tr>
<tr>
<td>LVSD</td>
<td>Left Ventricular Systolic Dysfunction.</td>
</tr>
<tr>
<td>MEMI</td>
<td>Middle East Medical Index.</td>
</tr>
<tr>
<td>MEPO</td>
<td>Middle East Pharmaceutical Products.</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial Infarction.</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health.</td>
</tr>
<tr>
<td>NCEP</td>
<td>National Cholesterol Education Programme.</td>
</tr>
<tr>
<td>NGOs</td>
<td>Non-governmental Organisations.</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute of Clinical Excellence.</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care.</td>
</tr>
<tr>
<td>PNDs</td>
<td>Paroxysmal Nocturnal Dyspnea.</td>
</tr>
<tr>
<td>PTCA</td>
<td>Percutaneous Transluminal Coronary Angioplasty.</td>
</tr>
<tr>
<td>RMS</td>
<td>Royal Medical Services of the Jordanian Army.</td>
</tr>
<tr>
<td>SA</td>
<td>Stable Angina.</td>
</tr>
<tr>
<td>SOB</td>
<td>Shortness of Breath.</td>
</tr>
<tr>
<td>TG</td>
<td>Triglycerides.</td>
</tr>
<tr>
<td>UNRWA</td>
<td>United Nations Relief and Works Agency.</td>
</tr>
<tr>
<td>UA/NSTEMI</td>
<td>Unstable Angina/Non-ST-Segment Elevation Myocardial Infarction.</td>
</tr>
<tr>
<td>WBC</td>
<td>White Blood Cells.</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation.</td>
</tr>
</tbody>
</table>
Preface

Why in Jordan?
The inspiration for this project arose primarily from two personal experiences of the researcher. First, the observation of prescribing practices and drug use at a general hospital in Jordan, which identified aspects of poor prescribing and drug use. This highlighted the need to evaluate clinical practice, and in particular to develop quality assessment measures. Second, the experience with foreign health care systems and witnessing UK clinical practice, which emphasised the importance of evidence-based practice, quality assurance frameworks, standardisation of care, and development of guidelines. Furthermore, the multi-professional approach to achieve optimal health outcomes, and safe, effective and rational medicine usage.

The scarcity of information in the literature on the Jordanian health infrastructure and clinical practice, further raised a desire to learn in depth about the Jordanian health model. An ambition to conduct a project to evaluate and eventually optimise clinical practice, specifically drug utilisation, developed. This was to fulfil an optimal goal of returning to Jordan to participate in teaching pharmacy students about their local health systems, how to apply evidence-based practice in local settings and to explore opportunities for the development of pharmacist role. The researcher noticed that pharmacy undergraduate curriculums taught in Jordan do not discuss the Jordanian health status, health care system or ongoing clinical practices. This alienates pharmacy graduates from local settings. They start their careers unaware of their health care system’s possibilities and limitations, or the opportunities for pharmacy development, which curtail their ability to function effectively. It is essential for practitioners to understand the systems they work in to be able to appraise and develop services to meet demand. Another goal of the research was to explore potential areas for pharmaceutical care services, as it would endorse their introduction to the system, because they were absent at the inception of the project.
Inception, Overall Aim and Objectives of the Project:
The research started in April 2000 with an overall aim to evaluate drug utilisation in
cardiac diseases at Jordanian hospitals. To provide indications on gaps in drug use
processes and propose recommendations to optimise prescribing. Furthermore, to
explore potential areas for pharmacists’ contributions in secondary care for cardiac
patients. However, the lack of up-to-date information on health conditions and
infrastructure in Jordan, rendered the exploration of these issues necessary. This was to
establish baseline data, which would serve as an introduction to the health care system,
and support the planning of the project. The project has the following objectives:
1- To describe health conditions and health care system in Jordan.
2- To describe drug use processes in cardiac diseases at Jordanian hospitals.
3- To develop a tool for the assessment of cardiovascular drug use in coronary heart
diseases and heart failure in Jordan.
4- To evaluate cardiovascular drug use through implementation of the developed tool,
identify gaps in practice and propose recommendations to optimise it, highlighting the
opportunities for pharmacists to assist in the care of cardiac patients.

The findings from carrying out each of the above objectives guided the execution of the
subsequent one. Hence, the planning of the project was sensitive to the local settings’
needs, which would enhance the benefits from the project.

Organisation of the Thesis:
The thesis is divided into two parts. The first part comprises chapters one and two,
which present a thorough overview of the Jordanian health conditions and the health
care system, based on the literature review and interviews with key health care
professionals in Jordan.

In chapter one, cardiovascular diseases (CVD), specifically coronary heart diseases
(CHD) are identified as the primary cause of death and the second leading cause of
hospitalisation in the Jordanian population. Further increase in the burden of CVD is
inevitable, in the light of several factors, primarily: the demographic shift of the
population towards aging, the high prevalence of CVD risk factors, and the inadequate public health awareness.

The Jordanian health care system is composed of multiple health providers with no single managerial body. It is primarily composed of the public and the private health sectors, which differ considerably in terms of resources, manpower, and medical technology. Health expenditure in Jordan is among the highest in the region, with hospital services and pharmaceuticals being the most expensive elements of health care.

The literature review has identified many gaps, particularly in terms of health care at secondary level, the role of pharmacist in patient care, drug utilisation processes and the factors which influence prescribing practices. For this purpose, interviews with key health care professionals were conducted to close the literature gaps, as presented in chapter two. Valuable information was generated, which further guided the planning of the project. Most notably are the reports on irrational prescribing patterns and prevailing branded prescribing practices, the absence of local treatment guidelines, and the lack of active role for hospital pharmacists in patient care. Furthermore, the factors which impede drug use, patient care and counselling on medication, particularly in the public health sector, which raised speculations on the appropriateness of drug use patterns. However, as there were no information available on actual drug use practices, the project was steered into a clinical, patient-oriented direction to investigate the CV drug prescribing and monitoring patterns in Jordanian hospitals as shown in the second part of the thesis.

The second part comprises chapters three, four, five and six, which involve the description and evaluation of CV drug utilisation in Jordanian hospitals. Chapter three presents the evidence on the benefits of CV medication use in the management of CVD and the effective role played by pharmacists in patient care in international settings. Furthermore, it discusses the different approaches and methods to the evaluation of drug use, which assisted the planning of the evaluation of CV drug utilisation undertaken in the project.
Chapter four presents an exploratory study of CV drug utilisation patterns in cardiac diseases in three Jordanian hospitals from different sectors. It is considered the first study to describe cardiovascular drug use and prescribing patterns in hospitals in Jordan. The patterns of CV drug prescribing, dosing, and monitoring are identified. However, the appropriateness of practice was not investigated. Therefore, the development of a tool for the assessment of CV drug utilisation evolved, as presented in the following chapter.

Chapter five discusses the development of local treatment guidelines to evaluate CV drug utilisation practices in Jordanian settings. The importance of involving practitioners in developing practice evaluation standards is emphasised, due to the strong ownership of practice by physicians, as the case in most of the developing countries. Tailoring the guidelines to the local settings' needs is also discussed, which is important to assure their validity in assessing local practices.

In chapter six, the Jordanian practice of CV drug use is evaluated using the developed guidelines. Indications on the gaps in drug prescribing, monitoring and follow up of cardiac patients are presented. Recommendations to improve the current drug use practices are proposed, highlighting the considerable role which could be played by the pharmacists to optimise cardiac patient care at secondary level.

The final chapter in the thesis, chapter seven, provides an overall discussion of the thesis and highlights areas for practice improvement and opportunities for pharmacists in patient care. Finally, the references and appendixes are listed at the end of the thesis. Most notable is appendix (10), which presents the templates developed for the evaluation of CV drug use at the Jordanian settings.
Chapter One:

Health Conditions in Jordan and the Jordanian Health Care System.

Introduction:
This chapter provides an up-to-date comprehensive overview of health conditions and health care system in Jordan. It has the objectives of describing the following:

- The Jordanian population in terms of demography and epidemiology profiles, pointing out the major health problems.
- The health care system structure and performance, highlighting health care services’ comprehensiveness, population coverage, delivery, accessibility and effectiveness.
- The health insurance schemes, their population coverage and eligibility.
- The pharmaceutical sector, its structure, services and performance.

This information provided a baseline, which supported the planning of the project. It allowed identifying priority diseases to investigate. It presented the different health sectors and facilities, which informed the choice of the study settings. It also gave an idea about the ongoing pharmaceutical services. A thorough literature review was conducted to fulfil the above objectives. Methods of searching the literature are stated below.

Methods of Literature Review:
Several information sources were used to complement each other and to locate unpublished studies and those not listed by electronic databases. The PubMed/Medline (1965-2006) and IPA (1970-2006) databases were searched for studies on Jordan. Abstracts were reviewed and studies relevant to health conditions, infrastructure, HCPs, and public health awareness were obtained. Additionally, Jordanian websites and several online library catalogues were searched for information on Jordan’s population, health status and health care system. Hand search of key journals pertinent to international health affairs, especially in developing countries, was also conducted. It covered the following journals:
Several governmental, non-governmental, and academic bodies in Jordan were contacted to obtain relevant studies and reports. These were the Ministry of Health (MOH), the Drug Department, the Primary Health Care Department, the Health Education Department, the Disease Control Directorate, the Department of Research, the Department of Statistics (DOS) and the MOH Information Centre. In addition to the University of Jordan, the National Centre for Diabetes, Endocrine and Genetic diseases, the Jordanian Pharmaceutical Association, the United Nations Relief and Works Agency (UNRWA) and World Health Organisation (WHO) offices in Amman.

Recently the MOH created an electronic database, which provides information on the population demography, morbidity, mortality and health infrastructure. It was searched in 2004, and the search was repeated in 2006 for updated information.

The Hashemite Kingdom of Jordan:

Demography of the Population:
Jordan is a small country in the heart of the Middle East. The government is a constitutional monarchy. Amman is the capital city (CIA, 2006).

Conflicting estimations of the population exist. The latest estimation by the government was a 5.3 million population in the year 2004 (DOS, 2005). Whereas, the WHO Eastern Mediterranean Regional Office (EMRO) reported a population of 5.6 million in the year 2004 (EMRO, 2005). More recent sources reported a population of 5.7 million in 2005 (CIA, 2006). The population is a mixture of communities and religions, predominantly Arabs who constitute 98% of the population. In addition to Circassians (Muslims of the Northwest Caucasus) and Armenians, each forming 1% of the population (CIA, 2006).
The population can be classified into urban, rural, Palestinian refugees, bedouins, and gypsies. Islam and Christianity are the two main religions practised, with Muslims constituting 92% of the population (CIA, 2006).

The population is mainly young-adult, however trends in age group distribution are shifting towards aging. This was attributed to improved health care and disease control measures (World Bank, 1997; WHO, 2003). For example, in 2000, 38% of the population were under the age of 15, 59% were between 15-64 years old, and 3% were above 64 years old (CIA, 2000). In 2004, the people under 15 dropped to 37.1%, whereas those above 64 years old increased to 3.8% (DOS, 2005). More characteristics of the Jordanian population are shown in table (1) for the years 1999 and 2004.

The past decades showed an increase in urbanisation, from 46% in 1965 to 82% in 2004, also a substantial improvement in accessibility to safe water and sanitation (DOS, 2005; EMRO, 2005; Makhlof et al, 1993). Similarly, literacy rates rapidly increased to reach 90% in 2004 (DOS, 2005).

Although the country particularly the capital city looks affluent and modern, poverty and unemployment are major problems. Absolute poverty rate was estimated at 26% in 1997, rising up to 30% in 2001 (Mamser, 1998; CIA, 2006). Unemployment rate was estimated at 12.5-13% in 2004 (DOS, 2005; EMRO, 2005), however, an unofficial rate of 30% was reported (CIA, 2006). The gap between the different social classes is widening, ranging from elite urban residing in modern areas to Palestinian refugees living in poor-status camps, or bedouins and gypsies living in underdeveloped rural areas. These problems were aggravated by the return of expatriates after the Gulf war in 1990 (World Bank, 1997), and foreigners who fled into the country after the war on Iraq in 2003. This has also put great pressure on the already strained economy and infrastructure.
Table (1): Health and Socioeconomic Indicators of the Jordanian Population in 1999 and 2004:

<table>
<thead>
<tr>
<th>Indicator</th>
<th>1999</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude birth rate (per 1000 population)</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>Crude death rate (per 1000 population)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Infant mortality rate (per 1000 live births)</td>
<td>28</td>
<td>24</td>
</tr>
<tr>
<td>Maternal mortality rate (per 10,000 live births)</td>
<td>4</td>
<td>4*</td>
</tr>
<tr>
<td>Total Fertility rate</td>
<td>3.82</td>
<td>3.7</td>
</tr>
<tr>
<td>Average persons per family</td>
<td>6</td>
<td>5.4</td>
</tr>
<tr>
<td>Population growth rate (%)</td>
<td>3</td>
<td>2.6</td>
</tr>
<tr>
<td>Life expectancy at birth (Male)</td>
<td>69</td>
<td>70.6</td>
</tr>
<tr>
<td>Life expectancy at birth (Female)</td>
<td>71</td>
<td>72.4</td>
</tr>
<tr>
<td>Adult literacy rate* Male</td>
<td>93.5</td>
<td>94.4</td>
</tr>
<tr>
<td>Adult literacy rate* Female</td>
<td>81.6</td>
<td>84.9</td>
</tr>
<tr>
<td>Unemployment rate</td>
<td>14.4</td>
<td>12.5</td>
</tr>
<tr>
<td>GDP per Capita (JD)</td>
<td>1110</td>
<td>1515.6</td>
</tr>
<tr>
<td>Population below poverty line (%)</td>
<td>30 †</td>
<td>30 †</td>
</tr>
</tbody>
</table>

JD: Jordanian Dinars.
* Source: MOH, 1999; DOS, 2005.
* Source EMRO (2005), for the year 2004.
* For individuals ≥15 years old.

Health Status and Epidemiology:
The health status in Jordan is improving (WHO, 2000; Hijazi, 2005), yet the picture is not very clear. This is due to several factors:

- First, the programs of monitoring health conditions, mortality and morbidity patterns are not well-structured. The MOH disease surveillance systems are generally weak, except for some noticeable communicable diseases (Disease Control Directorate, 1999).
Second, public health care facilities records are often incomplete and of questionable accuracy. Hence, they are unreliable. The lack of accurate data on mortality rates and causes of death has been stated by different sources (Hijazi, 2005; Khoury et al, 1999; World Bank, 1997).

Third, information on the private health sector, which is a major health provider, is limited. For example, although all private health care providers are obliged by law to report cases of communicable diseases to the MOH, only few comply, which further adds to the ambiguity of the current health situation (MOH, 1996).

In light of the above, a number of large surveys were conducted to establish reliable data on mortality and morbidity rates and patterns. Furthermore, some smaller-scale studies on disease prevalence, as well as health reports and screening procedures have contributed to the understanding of the epidemiological profile in Jordan.

Mortality and Morbidity Patterns:

Mortality Rates and Causes of Death:
Mortality rate is an important indicator to assess health conditions. In Jordan, mortality rates have shown a rapid decline over the past few decades (Hijazi, 2005; Anonymous, 2000; CIHI, 1996; Makhlof et al, 1993; Anonymous, 1992). Crude death rate dropped from 23 per 1000 population in 1960 to 5 deaths per 1000 population in 2004 (CIHI, 1996; DOS, 2005). Nonetheless, mortality is under-reported and up to half of deaths are unregistered (Hijazi, 2005; Khoury et al, 1999; World Bank, 1997). Furthermore, the causes of death are inaccurate and misinterpreted (Hijazi, 2005; Khoury et al, 1999). To obtain reliable estimates, a large study was conducted to identify mortality rates and causes of death (Khoury et al, 1995-96). A random sample of almost 200,000 individuals representing all population groups was included. Nine hundred and sixty five deaths were detected. While Khoury et al (1995-1996) identified the definite cause of death in 93% of cases, screening the MOH records showed that 40% of the registered deaths were ascribed to ill-defined conditions, and another 40% to cardiovascular (CV) causes. Moreover, further scrutinising of the CV deaths revealed that the mode rather
than the cause of death was documented, which indicated the considerable misinterpretation of causes of death in the MOH records.

The three leading causes of death were circulatory system diseases, neoplasm and accidents, causing 41.97%, 12.58% and 10.47% of all deaths, respectively (Khoury et al, 1995-96; Khoury et al, 1999). This is similar to the leading causes of death in the UK, except for the third cause, which is respiratory system diseases, as shown in table (2).

Cardiovascular diseases (CVD) and cerebrovascular accident (CVA) were the major circulatory system diseases causing mortality in Jordan, where myocardial infarction (MI) constituted 50% (73% men, 27% women), CVA 33.5% (52% in men and 48% in women), and chronic ischemic heart diseases (IHD) 9.9% (76% in men and 24% in women) (Khoury et al, 1995-96; Khoury et al, 1999). Hypertension (HTN), diabetes mellitus (DM), and IHD were considered the major contributing factors of death in MI patients (Khoury et al, 1995-96).

Cancer was more prevalent in men than in women (53% vs 47%). Lung cancer was the most prevalent in men causing 17.5% of all cases, whereas in women breast cancer caused 30% of cases (MOH, 1999).

*Morbidity Rates and Patterns:*
The morbidity profile is not very clear, as explained earlier, particularly for non-communicable diseases. On the contrary, communicable diseases gain substantial attention from the health authorities.

*Non-communicable Diseases:*
The MOH conducted a large survey to develop an accurate epidemiological profile and describe changes in morbidity patterns (MOH, 1996). The prevalence of risk factors such as hypertension, diabetes, hypercholesterolaemia, obesity, smoking, and physical inactivity was investigated. The incidence and prevalence of morbidity of all causes in the community and health care facilities were also investigated. The risk factors survey
included 2435 adults (25 years old and over) from three different regions. The sample was not representative of the population in terms of age, sex, and education, except for geographical distribution. The survey showed high prevalence of risk factors, where 32% of the sample had hypertension (HTN), 46% had hypercholesterolaemia, 7% had DM, 25% were physically inactive during work hours and 70% were overweight.

### Table (2): Epidemiological Profile of Cardiovascular Diseases in the UK *

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality (in thousands, year 2004)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>244,130</td>
<td>268,411</td>
</tr>
<tr>
<td>Circulatory system diseases</td>
<td>91,163</td>
<td>99,440</td>
</tr>
<tr>
<td>Chronic IHD</td>
<td>29,085</td>
<td>23,779</td>
</tr>
<tr>
<td>Acute MI</td>
<td>22,054</td>
<td>17,161</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>72,156</td>
<td>65,906</td>
</tr>
<tr>
<td>Respiratory system diseases</td>
<td>31,651</td>
<td>37,562</td>
</tr>
<tr>
<td><strong>Morbidity</strong> (year 2003)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD diagnosed</td>
<td>13.6%</td>
<td>13.0%</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>3.8%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Angina</td>
<td>4.8%</td>
<td>3.4%</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 2003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension*</td>
<td>31.7%</td>
<td>29.5%</td>
</tr>
<tr>
<td>Hypertension treatment rates</td>
<td>36.8%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Diabetes Mellitus (type I and II)</td>
<td>4.8%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Physical activity**</td>
<td>79.0%</td>
<td>74.0%</td>
</tr>
<tr>
<td>Year 2004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>23.6%</td>
<td>23.8%</td>
</tr>
<tr>
<td>Smoking (current smokers)</td>
<td>22.0%</td>
<td>23.0%</td>
</tr>
<tr>
<td>Population achieving the recommended physical activity target***</td>
<td>35.0%</td>
<td>24.0%</td>
</tr>
</tbody>
</table>

* Source of data: National health statistical reports.

* Defined as SBP ≥140mmHg, DBP ≥ 90mmHg, or taking drugs for high blood pressure.

** Defined as any physical activity of at least moderate intensity for at least 30 continuous minutes.

*** Recommended activity target: any activity of at least moderate intensity for at least 30 minutes on at least 5 days a week.
Moreover, 25% of the sample were current smokers and half of the non-smokers were passive smokers. These figures are comparable to the prevalence of CVD risk factors in the UK, except for a much higher obesity and slightly higher DM rates in the Jordanian population (table 2).

The risk factors survey also found considerable unawareness of the public on their health. For instance, only 9% of the sample classified themselves as hypertensive, whereas physical examination proved HTN in 32%, which was severe in 50% of these cases. Similarly, only 2% of the sample thought they had high cholesterol levels, which was notably different from the above mentioned figure of 46% (MOH, 1996).

The morbidity survey included almost 7000 adult Jordanians (25 years and over) residing in three different regions. The study cohort was contacted in the middle of each season, over a one year period, and followed up for 2 weeks, to detect new morbidity incidents. The incidence and prevalence of morbidity in the community and health care facilities, at regional and national levels, as well as seasonal and regional variations in morbidity patterns were investigated. The overall morbidity incidence rate peaked in winter, while the prevalence rate was highest in Autumn (figure 1).

Figure (1): Overall Morbidity Prevalence and Incidence Rates (MOH, 1996).

In the community, respiratory system diseases were the most incident and most prevalent diseases in all seasons. They accounted for 25% of the detected diseases and 50-70% of the new incidents, being highest in Winter. Circulatory system diseases were
the second most prevalent diseases followed by musculo-skeletal, digestive system, eye and ear diseases. While the second most incident diseases were digestive system and genitourinary diseases in Winter, ear, eye and infectious diseases in Spring, Summer and Autumn.

In outpatient departments, the respiratory system diseases were the leading cause of morbidity in all seasons at both regional and national levels. These were followed by circulatory system diseases, ear and eye diseases. As for hospitalisation, at a national level, pregnancy and labour were the leading cause of hospitalisation in all seasons followed by circulatory system diseases, except in Autumn where mental health problems were the second leading cause of hospitalisation (MOH, 1996).

The prevalence of non-communicable diseases was also investigated by some smaller clinical studies. Ajlouni et al (1998a) investigated the prevalence of DM, impaired glucose tolerance (IGT) and related risk factors in 2836 adult individuals. The prevalence of DM was 13.4%, exceeding the rate of the MOH survey (1996) and in other countries in the region (WHO, 2006). IGT was reported in 9.8%, HTN in 15%, hypercholesterolaemia in 30% and hypertriglyceridaemia in 26% of the sample. The study group predicted significant increase in the prevalence of DM in the future, because of the high prevalence of risk factors, change in life-style and demographic transition of the population towards aging (Ajlouni et al, 1998a). Obesity was also investigated in the same sample and was evident in 50% of cases (Ajlouni et al, 1998b). Obesity rates in Jordan exceeds that in other neighbouring countries (Khatib, 2004). In 1996, the prevalence of HTN investigated in 2299 adult Jordanians reached 16.1%. Half of the patients were unaware of their HTN, regardless of their gender or educational level. Furthermore, 36% of those aware of their condition had uncontrolled elevated blood pressure (Jaddou et al, 1996). A more recent study, in 2000, reported a similar prevalence rate of HTN of 16.3%. However, the awareness on having HTN had increased to 82% of patients, yet 68% of them had uncontrolled blood pressure levels (Jaddou et al, 2000). This signified increased public awareness on their health status, yet their poor knowledge of disease management.
All of the above studies recommended further investigation of the prevalence of diseases and risk factors in other population groups. The need to increase public awareness on diseases, healthy lifestyles, diets, physical activity, and smoking cessation was emphasised (Jaddou et al, 2000; Ajlouni et al, 1998a; Ajlouni et al, 1998b; Batieha et al, 1997; Jaddou et al, 1996).

*Communicable Diseases:*
Infectious diseases are among the main causes of death (Hijazi, 2005). The MOH exerts considerable efforts to monitor, prevent and control communicable diseases. This is to prevent epidemics, particularly in overcrowded and poor areas. There are around 40 communicable diseases, which the MOH screens annually. In the 1999 MOH report diarrhea was the most incident disease, followed by mumps, chicken pox, animal bites, hepatitis A, scabies, meningitis, measles, and TB. The incidence rate of all diseases peaked in the hot seasons. For almost all of the diseases, the incidence rate was higher in males, and Children and youth under 20 years old were the most affected groups. There is a decrease in the incidence of some communicable diseases over time, as shown from comparing rates in the years 1997, 1998 and 1999. This could be attributed to the immunisation programs regularly launched by the MOH, which were successful in controlling diseases, particularly poliomyelitis, diphtheria, pertussis, and tetanus. Some diseases were successfully eradicated, such as typhus, cholera, and plague (Disease Control Directorate, 1999).

Jordan is seen to be entering an epidemiological transition phase characterised by:
- Rapid decrease in mortality and increased life expectancy.
- Increase in non-communicable diseases.
- Continuing increase in the incidence of infectious diseases.
- Unequal distribution of wealth and population coverage leading to widening the gap in health status among the different income groups and regions. As a result, epidemiological polarisation evolves, which may lead to re-emergence of previously eradicated diseases (World Bank, 1997; WHO, 2000).
Health Awareness in the Community:
Few studies investigated health awareness and behaviours, which were limited to certain health topics and population groups. Al Ma’aitah et al (1999) investigated health promotion behaviour among Jordanian women and concluded that little attention was given to health promotion in comparison to disease prevention and treatment measures. The study emphasised the need to investigate lifestyle, diet and exercise patterns, as a prerequisite for effective planning of public health awareness strategies. On the other hand, public unawareness of their health conditions or the appropriate disease prevention and management measures were reported by several studies (Jaddou et al, 2003; Jadalla et al, 1998; MOH, 1996; Janson et al, 1994; Nazer et al, 1993). The unawareness among cancer patients on their disease prevented appropriate action and prompt seeking of medical consultation (Jadalla et al, 1998).

The government regularly launches public awareness campaigns on major health problems such as accidents, cancer, smoking and food safety (Kandela, 2000; Jadalla et al, 1998; Dajani et al, 1989). Unfortunately, the literature evaluating the outcome of these campaigns is limited. However, indicators show that some of these campaigns attained a positive change such as family planning and birth spacing campaigns. While other campaigns did not achieve their goal like the smoking cessation one (Kandela, 2000). In 2003, the Global Youth Tobacco Survey found 33% of students were current smokers (GYTS, 2003).

The need for education and counselling programs on different health-related topics, e.g. accidents, home safety, cancer, myocardial infarction, nutrition, smoking, prevention and management of diseases has been emphasised (Al-Hassan and Omran, 2005; Al-Ma’aitah et al, 1999; Al-Kharabsheh et al, 1999; Jadalla et al, 1998; Jaddou et al, 1996; MOH, 1996; Janson et al, 1994; Makhlouf et al, 1993; Nazer et al, 1993).

Drug Misuse in the Community:
This brief paragraph was included out of believing how important yet under-reported drug misuse is in Jordan. There are very few studies that investigated drug use by HCPs.
and/or patients in Jordan. A recent study revealed low awareness of the community on use of NSAIDs (Albsoul-Younes et al, 2004). Otoom et al (2002a) reported excessive use of antibiotics by prescribers at primary care level. This endorsed previous reports on increasing bacterial resistance, which was ascribed to indiscriminate antibiotic use (Rawashdeh et al, 1994; Dajani et al, 1989; Khuri-Bolus et al, 1988). It also could be explained by the free public accessibility to medication without prescriptions. Unless strict strategies are implemented to control drug use and enhance patient awareness, the problem will continue leading to inevitable negative health outcomes.

**Key Points on Health Conditions in Jordan:**

- Demographic transition of the population towards aging with improved health conditions.
- Circulatory system diseases are the leading cause of death in Jordan, primarily cardiovascular diseases (MI and chronic CHD). They are also the second most prevalent diseases and the second leading cause of hospitalisation.
- Risk factors for cardiac diseases such as HTN, DM, obesity, physical inactivity, dyslipidaemia and smoking are prevalent among adult Jordanians.
- Jordanians’ awareness on their health status, disease prevention and management is low. Effective public educational campaigns are crucial.
- Easy accessibility to medication without prescriptions, encourages drug overuse and indiscriminate self administration. Strict rules to control drug use must be enforced.
Chapter One

The Jordanian Health Care System:
This section discusses the Jordanian health care system, its structure, services, and performance, as well as health insurance schemes. Moreover, it presents the pharmaceutical sector, its structure and performance, and highlights its conditions and limitations.

Structure of the Health Care System:
The health care system is formed of several health care programs. It is divided into public and private health care sectors (figure, 2). The public sector comprises two major health care programs, the Ministry of Health (MOH) and the Royal Medical Services of the Jordanian army (RMS) programs. In addition to a smaller health program provided by the university. The private sector consists of privately owned health care facilities, as well as those run by non-governmental organisations (NGOs), primarily the United Nations Relief and Works Agency (UNRWA).

1. The Public Health Sector:

1.1 The MOH Health Program:
The MOH is the major health authority in the country. Since its foundation in 1950, the MOH has been responsible for legislat ing all health-related affairs. It also finances and administers the largest public health care program and the civil insurance program. It owns an extensive net of public health care centres (HCC) and 29% of hospitals (total number of hospitals in Jordan =100). Moreover, it employs 27% of physicians, 22.3% of nurses and 3.3% of pharmacists (table, 3) (MOH, 2004). Allocation of resources within the MOH program is highly centralised. Individual facilities do not have their own budgets, alternatively they receive supplies, equipment, and pharmaceuticals from central MOH departments (World Bank, 1997; WHO, 2003). Health care professionals (HCPs) are salaried with income levels that are much lower than in the private sector.
Figure (2): Structure of the Jordanian Health Care System:

The Health Care System

Public Sector

- MOH Health Program
  - Public Hospitals
  - Health Care Centres
  - Primary
  - Comprehensive
  - Mother and child

- RMS (army) Health Program
  - Hospitals
  - Health Care Centres
  - Peripheral
  - Dental Clinics

- Jordan University Hospital and King Abdullah University Hospital (Opened Nov 2002)

Private Sector

- Private Health Program
  - Hospitals
  - Dental Clinics
  - Single-handed Clinics

- NGOs
  - UNRWA Health Program
  - Primary Care Facilities
  - Rehabilitation Centres
Chapter One

The MOH program is the largest public health program in terms of expenditure. In 1998, it was estimated at JD 149 millions, constituting 33% of total health expenditure. It covers 23% of the population (JNHA, 2000). These are civil employees, their dependants, blood donors, disabled citizens and those classified as poor. Health care is provided to these groups free or at nominal charge in MOH premises. However, any citizen can refer to the MOH facilities, even if covered by other health programs or uninsured (JNHA, 2000). Unless patients are insured, they bear the full costs of services. However, services at the MOH facilities are highly subsidised in comparison to other sectors.

1.2 The RMS Health Program:
This is the second largest public health program in terms of expenditure. Yet, it is the largest program in terms of population coverage. In 1998, RMS health expenditure accounted for 15% of total health expenditure (JNHA, 2000). It covers 35% of the population. These are military employees and their dependants (JNHA, 2000). They receive free health care services at the RMS facilities. Citizens covered by other health programs can also use the RMS hospitals. However, non-military personnel bear service charges, which could be covered either exclusively or partially by insurance. The RMS operates several ambulatory centres and 10% of hospitals. It employs 9% of physicians, 10% of nurses and 3% of pharmacists (table, 3) (MOH, 2004). Similar to the MOH, allocation of resources to the RMS facilities is highly centralised, and its employees are salaried (World Bank, 1997; WHO, 2003).

1.3 The University Health Program:
This is the smallest public health program in terms of expenditure, number of facilities, and population coverage. It constituted 5% of total health spending in 1998 (JNHA, 2000). It owns 2 hospitals, the Jordan University Hospital (JUH), which is run by the Jordan University and -recently- the King Abdullah University Hospital (KAUH), which is run by the Jordan University of Science and Technology (figure, 2). It covers university staff, their dependents, and students (around 0.5% if population in 1998) (JNHA, 2000). They receive services free of charge or at highly subsidised costs. The
rest of the population can use the hospital on a fee-for-service basis (WHO, 2003). The program employs 3.6% of physicians, 0.7% of nurses and 0.5% of pharmacists (table, 3) (MOH, 2004). Management of the program is centralised and employees are salaried.

2. The Private Health Sector:
The private sector comprises the increasingly expanding private health program, in addition to smaller programs provided by NGOs, primarily UNRWA (figure, 2).

2.1 The Private Health Program:
In 2002, the private program accounted for 54% of total health expenditure and 30% of service delivery (WHO, 2005; Hijazi and Al-Ma'aitah, 1999). All citizens who can afford private services costs can refer to private health facilities. Services are purchased through out-of-pocket payment, unless patients are insured. The program owns 59% of hospitals and attracts the majority of health manpower (table, 3), because of better incentives and higher income levels. Staff is either salaried or reimbursed on a fee-per-service basis (JNHA, 2000). The program employs 60% of physicians, 60% of nurses and 93% of pharmacists (MOH, 2004). Generally, information on the private health sector spending, capacity and utilisation is limited. The Jordan Healthcare Utilization and Expenditure Survey (JHUES), however, found that 40% of outpatient visits and 21% of inpatient visits took place at private facilities, compared to 49% and 55% at the MOH, respectively (JHUES, 2000).

2.2 The NGOs Health Program (The UNRWA Program):
UNRWA is the major NGO in Jordan, serving Palestinian refugees, whose number is estimated at 1.74 million registered refugees (UNRWA, 2003). UNRWA health program accounted for 2% of total health spending in 1998 (JNHA, 2000). The organisation runs 23 primary health care and rehabilitation centres (UNRWA, 2003). It employs 95 physicians, 42 nurses and 2 pharmacists (MOH, 2004). Patients who need secondary or tertiary health care are referred to the MOH or private hospitals (UNRWA, 2003).
Table (3): Health Manpower and the Hospital Sector in Jordan*:

| Sector   | No. of hospitals | No. of beds | Occupancy rate | No. of admissions (%) | No. of admissions | Average LOS | Death rate | No of outpatient visits (%) | No of outpatient visits | Average LOS | Death rate | No of outpatient visits | No of outpatient visits | Average LOS | Death rate | No of outpatient visits | No of outpatient visits | Average LOS | Death rate | No of outpatient visits | No of outpatient visits |
|----------|------------------|-------------|----------------|-----------------------|-------------------|-------------|------------|-----------------------------|------------------------|-------------|------------|-----------------------------|------------------------|-------------|------------|-----------------------------|------------------------|-------------|------------|-----------------------------|------------------------|-------------|------------|-----------------------------|------------------------|
| MOH      | 29               | 3606        | 69.4           | 271,866 (42)          | 3.2               | 1.4         |            | 2,352,115 (45.5)             | 3250 (27.1)            |            |            | 224 (3.3)                   |            |            |            |            |            |
| RMS      | 10               | 1848        | 77             | 120,909 (18.5)        | 4.4               | 2.4         |            | 1,848,340 (35.7)             | 1082 (9.0)             |            |            | 201 (2.9)                   |            |            |            |            |            |
| University |                |             |                |                      |                   |             |            |                             |                        |             |            |                             |                        |             |            |                             |                        |             |            |                             |                        |
| JUH      | 1                | 535         | 72.9           | 27,376 (6.2)          | 5.2               | 2.2         |            | 320,888 (6.2)                | 294 (2.4)              |            |            | 18 (0.3)                    |            |            |            |            |            |
| KAUH     | 1                | 304         | 72.7           | 19,873 (2.6)          | 4.1               | 1.7         |            | 135,131 (2.6)                | 149 (1.2)              |            |            | 13 (0.2)                    |            |            |            |            |            |
| Private  | 59               | 3569        | 43.1           | 212,910 (32)          | 2.6               | 0.8         |            | 511,047 (9.8)                | 7138 (59.5)            |            |            | 6277 (93.2)                 |            |            |            |            |            |
| UNRWA    | 0                | 0           | --             | --                    | --                | --          |            | --                          | 95 (0.8)               |            |            | 2 (0.03)                    |            |            |            |            |            |
| Total    | 100              | 9862        | 62             | 652,934 (100)         | 3.3               | 1.4         |            | 5,167,521 (100)              | 12,008 (100)           |            |            | 6735 (100)                  |            |            |            |            |            |

JUH: Jordan University Hospital. LOS: Length of stay. KAUH: King Abdullah University Hospital.

**Health Care Facilities and Services:**

The health care system comprises an extensive network of health care facilities; public and private, at primary, secondary and tertiary levels. A wide range of services is offered; preventive, curative, and pharmaceutical. Health care facilities are mainly classified into health care centres and hospitals. The role and use of these facilities are described below.

1. **Health Care Centres (HCC):**

HCC are mainly public facilities, the majority of which are affiliated to the MOH (JNHA, 2000). In 2004, the number of MOH/HCC reached 1017 (MOH, 2004), the classification of which is depicted in figure (2). Additionally, there are more than 80 RMS/HCC (JNHA, 2000) and 23 UNRWA/HCC (UNRWA, 2003). The highest proportion of centres is in the capital city, yet regional variations in distribution exist. However, population coverage is almost absolute; ranging from 96-100% (EMRO, 2005).

HCC offer primary health care services, such as reproductive health, family planning, mother and child health, immunisation, dental care and provision of drugs (Qubein et al, 1988; Hijazi and Al-Ma’aitah, 1999; WHO, 2003; Khoury and Mawajdeh, 2004). In 2004, the number of visits to the MOH primary HCC reached 9.4 million. Respiratory diseases were the leading cause HCC visits followed by digestive system diseases, accounting for 42% and 9.2% of visits, respectively (MOH, 2004).

Although HCC are considered the first point of contact with the health care system, many patients refer to hospitals as a first contact, which is resulting in overutilisation of hospitals and high expenses (Abdallat et al, 2000). It could be explained by the reported low quality of services and inadequate equipping of HCC (Hijazi and Al-Ma’aitah, 1999; Qubein et al, 1988).

2. **Hospitals:**

Total number of hospitals in Jordan is 100, of an overall capacity of 9862 beds, and an
average occupancy rate of 62\% (MOH, 2004). The private sector owns the biggest number of hospitals with 59 hospitals, followed by the MOH with 29 hospitals, the RMS with 10 hospitals, and university with 2 hospitals (table, 3). The bed capacity is almost equal in both the private and MOH sectors, reaching in each 36\%, followed by the RMS (18\%) and the university (8.5\%). The number of hospitals is highest in the capital city, and the average bed: population ratio is 18 per 10,000 (MOH, 2004).

Hospital occupancy rate is highest at the RMS at 77\%, followed by university at 73\%, and the MOH at 69.4\%. Whereas, it is lowest at private hospitals reaching 43\% (MOH, 2004). Average hospital length of stay is 3.3 days. The university hospitals had the longest hospitalisation periods, whereas RMS hospitals recorded the highest death rate. Both the hospital length of stay and death rate were lowest at the private sector (table, 3). Almost 80\% of outpatient visits occur at the MOH and RMS hospitals. Whereas 42\% and 32\% of inpatient admissions are at the MOH and private hospitals, respectively (table, 3). Number of surgical procedures is highest at private hospitals, followed by MOH, RMS, and university hospitals (MOH, 2004).

**Health Insurance Programmes:**
The multiple health insurance programs and the fact that many individuals are covered by more than one program complicates the analysis and planning of health insurance in Jordan. It also impedes accurate identification of numbers of uninsured, as well as fully and partially insured populations (JNHA, 2000). Universal health insurance does not exist. While 66\% of the population are insured -at least by one program in 60\% of them- 40\% of the population are uninsured (JHUES, 2000; WHO, 2003). The numbers do not add up due to multiple coverage in 6\% of the population (JHUES, 2000). The major public schemes are the civil insurance program run by the MOH, which covers 21\% of the population, and the military insurance scheme run by the RMS and covers 30\% of the population (WHO, 2003). Smaller insurance programs are provided by the university, UNRWA and private companies. Public insurance schemes cover all charges of medical care given that services are provided by the same health program that runs the insurance scheme. Otherwise, if patients use other public health programs, they will bear a minor share of cost. Higher costs accrue with patients’ self-referral, yet the
greater share is covered by insurance. In all cases, there is a cost sharing for pharmaceuticals. On the other hand, private insurance could be purchased by anyone who can afford it. It offers a wider range of benefits than public insurance schemes (World Bank, 1997). Many people buy private insurance to complement their coverage (JNHA, 2000). Uninsured populations can use public or private services and bear full costs. Over than half of the uninsured were reported to use private health care facilities as their first contact with the health care system (JNHA, 2000).

Acquisition of health insurance influences the utilisation of health care services, the type of health program sought and the hospital length of stay (LOS) (Mawajdeh et al, 1997; JNHA, 2000; JHUES, 2000). In the Jordan living conditions survey more insured outpatients chose public providers than uninsured patients who preferred private facilities (JNHA, 2000). As for inpatient admissions, Mawajdeh et al (1997) reported that insured patients had a longer hospital stay (3.3 days) than uninsured patients (3 days) independent of illness. This was particularly evident in the private sector. The study showed that insurance status along with hospital type affected the LOS by 1.5 days; suggesting that half of the LOS was due to factors other than the medical condition. It raised questions on the efficiency of hospital utilisation, especially that the majority of health expenditure in Jordan is hospital-related (Mawajdeh et al, 1997).

**Performance of the Health Care System:**

1. **Management and Coordination:**
The fact that the health care system is formed of multiple autonomous programs with no single managerial body to organise the overall system. Also the lack of coordination between the public and private sectors, and overlap in service provision. All of these are resulting in a two-tiered system, and challenging the organisation of the system (WHO, 2003; JNHA, 2000; World Bank, 1997).

Furthermore, inefficient implementation of health strategies is attributed to the high rate of changing the MOH cabinets. Health care plans adopted by one cabinet are usually
abandoned by the following one, which is disrupting the execution of plans (personal communication with a MOH official, 2000). Ideally, health strategies should be adopted rather than individuals' views, which vary depending on people's incentives and initiatives.

2. Financing and Expenditure:

Health expenditure in Jordan is one of the highest compared to Middle East and North African countries of similar GDP (JNHA, 2000). In 2004, health expenditure accounted for 9% of GDP (MOH, 2004). While the private sector constituted slightly more than half of total health spending, 46% of spending was in the public sector (WHO, 2005). In 2004, the MOH budget was estimated at JD 161 millions, comprising 6% of total government budget (MOH, 2004). Hospital care is the most expensive component of the MOH health expenditure, accounting for 64% of the MOH budget (personal communication with an official at the JFDA, February 2006). Information on hospital expenditure in the private sector is not available. Nonetheless, high hospital expenditure has been reported and ascribed to lack of an effective hospital referral system, hospital-based orientation of treatment and indiscriminate overuse of hospital services (Abdallat et al, 2000; JNHA, 2000; Hijazi and Al-Ma'a’ithah, 1999; Al-Kharabsheh et al, 1999; World Bank, 1997). Policies to encourage the public to attend HCC rather than hospitals have been advocated to curb expenditure (JNHA, 2000; Abdallat et al, 2000; Al-Kharabsheh et al, 1999). At the same time, the need to adequately equip centres and employ competent manpower in them have been emphasised (WHO, 2003; Hijazi and Al-Ma’a’ithah, 1999; Kharabsheh et al, 1999).

Generally, the system is facing a problem of limited resources and increasing demand. Continuous growth of the population, shifting towards aging, inefficiencies in resource allocation and health services delivery are all overloading the system financially, particularly public programs (WHO, 2003; World Bank, 1997). Competition between private and public sectors, and patients' preference for private services have further minimised public programs revenues. Consequently, the capacity and stability of public programs are negatively affected (JNHA, 2000; World Bank, 1997).
3. Manpower:
There is a total of 12,008 physicians, 9373 nurses and 6735 pharmacists practising in Jordan in 2004 (MOH, 2004). The higher income levels and more incentives in the private sector are resulting in manpower shift from the public sector (table, 3), leaving the latter struggling with under-staffing (Hijazi and Al-Ma’aitah, 1999). As an example, the number of nurses working in the MOH comprised 51% of all nurses in 1999. This percentage dropped in 2004 to 22% of nurses. Whereas it increased in the private sector from 27% in 1999 to 60% of nurses in 2004 (MOH, 1999; MOH, 2004).

4. Coverage and Accessibility:
The system is performing well in terms of population coverage and accessibility. This is particularly valid for primary health care. Accessibility to local health services in urban areas is absolute and in rural areas is 96% (EMRO, 2005). Average patient travel time to the nearest HCC is 30 minutes (WHO, 2003). On the other hand, access to secondary and tertiary care could be more difficult to rural residents. However, the small country size and patients’ eligibility to use different health programs overcome geographical constraints (WHO, 2003; World Bank, 1997).

5. Eligibility and Equity:
Generally any citizen can use the public and private health care services. Eligibility to obtain public health coverage is determined by profession or socio-economic status. Patients at the public sector can be referred between the three public health programs. Furthermore, many of the publicly covered citizens purchase services from the private sector (JNHA, 2000). This was proven by the fact that 53% of services are privately purchased although 68% of the population have inclusive public coverage (World Bank, 1997). This multiple eligibility, however, complicates the coverage of the population.

Equity of the system is questionable in that some citizens enjoy an inclusive health coverage, while others do not have any form of it. A considerable section of the uninsured using private services pay much higher out-of-pocket fees than the insured. Moreover, many government employees at lower positions are not classified as civil
officials, hence they are not eligible for insurance coverage. Another example of inequity is that the civil insurance program covers civil employees and their dependants for pharmaceuticals even those purchased from the private sector. Whereas the poor and disabled are covered for the pharmaceuticals only available at public premises, i.e. the pharmaceuticals purchased from the private sector are borne by these patients, who are actually less capable to pay than civil employees. Furthermore, there is a maximum cap on insurance premiums, thus those with higher income pay less in proportion to their salaries than those on lower income for the same services (WHO, 2003; JNHA, 2000; World Bank, 1997).

6. Comprehensiveness, Quality and Effectiveness:

Services in the private and RMS sectors are more comprehensive than in the MOH and university, because of the more resources (World Bank, 1997). Several major challenges exist for the quality and effectiveness of health care services. These are:

- Research on the quality and effectiveness of health care services is scarce.
- Audit systems do not exist and the enforcement of standards of care is low (WHO, 2003; JNHA, 2000; Hijazi and Al-Ma’aitah, 1999). Use of the more expensive private services by a majority of the uninsured as well as many of the publicly covered citizens may indicate a problem with the quality of public health services (JNHA, 2000; Hijazi and Al-Ma’aitah, 1999; World Bank, 1997).
- Inefficiencies exist in organising and delivering health care services. There is an undue concentration on expensive curative services rather than preventive ones (WHO, 2003; JNHA, 2000; World Bank, 1997). Planning of the hospital sector does not match the public’s need. This is indicated by the low hospital occupancy rate signalling a redundant excess capacity.
- Over-utilisation of hospitals is enhanced by ineffective referral systems and the public using hospitals as their first contact rather than HCC (JNHA, 2000; Hijazi and Al-Ma’aitah, 1999; World Bank, 1997). Mawajdeh et al (1997) reported that length of stay at public hospitals was higher than in private hospitals, due to factors other than medical condition. The study raised questions on efficiency of utilising public hospitals. The study by Abdallat et al (2000), further confirmed
inappropriate use of hospitals. It found that 91% of cases admitted to emergency rooms in one military hospital were not urgent.

If the current policies of the health care system persists, increasing costs, accessibility gaps for vulnerable population, wasteful redundant capacity, and defects in health care planning and organisation are predicted (WHO, 2003; JNHA, 2000; Hijazi and Al-Ma’aithah, 1999; World Bank, 1997).

The Pharmaceutical Sector:

1. Structure and Regulation:
The pharmaceutical sector is chiefly regulated by the Jordan Food and Drug Administration (JFDA), which is responsible for legislating and administering drug-related affairs, such as registration, importation and exportation. The Jordanian Pharmaceutical Association (PA) collaborates with the JFDA and the MOH. However, its role is mainly advisory (personal communication with a PA official, 2000).

The sector comprises several autonomous pharmaceutical procurement and management systems. Each system is run by one of the health care programs mentioned earlier. There is an extensive network of pharmaceutical facilities, which are classified into pharmacies, drugstores and factories. In 2004, there were 1616 pharmacies, 213 drugstores and 20 local pharmaceutical factories (MOH, 2004). Pharmacies are classified into public and private pharmacies. The public pharmacies are privately owned and sell medication to the public at prices determined by the JFDA. A prescription is not needed to dispense medication except for certain CNS drugs. The number of public pharmacies is continuously increasing, which -in the light of the limited market size- is exceeding the public demand (personal communication with a PA personnel, 2000). The private pharmacies, on the other hand, are affiliated to medical, academic, social or charitable foundations. An example is outpatient and inpatient pharmacies at the MOH, RMS and university hospitals, as well as NGOs. They only serve population groups using these particular premises. The private pharmacies in
public and NGOs facilities dispense drugs only on prescription at nominal prices (personal communication with PA personnel, 2000).

Drugstores import medication and supply all pharmacies and hospitals at prices approved by the authorities. On the other hand, locally manufactured pharmaceuticals constitute 26% of the public consumption (JFDA, 2003).

2. Expenditure:
Pharmaceutical expenditure in Jordan is high compared to other countries in the region (JNHA, 2000). In 1998, the expenditure on pharmaceuticals constituted 35% of total health expenditure and 3.2% of GDP, reaching JD 159 million (WHO, 2003; JNHA, 2000). In 2004, this figure exceeded JD 200 million (FDA, 2004; FDA, 2003). Almost 76% of the expenditure on pharmaceuticals is private, whereas 24% occurs in the public sector (JFDA, 2003; JNHA, 2000). Around 54% of public expenditure on pharmaceuticals occurred at the MOH, reaching JD 23 millions in 2004 (JFDA, 2004). Pharmaceutical consumption increases annually by 10.6%, with an average annual consumption per person of JD 38 (JFDA, 2003). Drug procurement in the public sector takes place through tenders, which provides drugs at competitive prices. Whereas, in the private sector drugs are purchased at considerably higher costs (JFDA, 2004).

3. Performance and Obstacles:
The multiplicity of drug procurement programs and lack of coordination among them are introducing inefficiencies into the management of the sector. The WHO and MOH developed a national drug policy in 1998 to serve as a framework for developing the sector, controlling drug procurement and strengthening initiatives for rational drug use (WHO, 2003; Otoom et al, 2002a). Nonetheless, indications on ineffective implementation of this policy are evident from the continuing increase in expenditure and reports on irrational drug use (WHO, 2003; Otoom et al, 2002a, Otoom et al, 2002b; JNHA, 2000). The high centralisation of pharmaceuticals allocation within the public sector weakens drug distribution and availability in the individual facilities, leading to drug shortages and/or redundancy. Serious drug shortages in the public sector also result
from delays in settling for drug tenders. In contrast, there are no drug availability problems in the private sector. Other obstacles, which hinder efficient consumption of pharmaceuticals and result in excessive costs include the following (WHO, 2003; JNHA, 2000; World Bank, 1997):

- Lack of treatment protocols at facility levels to guide prescribing patterns.
- Lack of incentives for cost-containment and resources rationalisation, which:
  a) in the public sector is due to high centralisation of drug procurement and the population coverage policies, where patients bear nominal costs. This eliminates cost-consciousness on part of the prescriber and the patient.
  b) in the private sector is influenced by providers making profit and patients’ coverage. Uninsured patients would accept cheaper drugs as they cover full costs of medication.
- Drug promotion and the prevailing branded prescribing habits. In an environment not oriented to generic prescribing, physicians tend to prescribe heavily promoted and expensive drugs, as they are not urged to rationalise therapy cost. Although generic prescribing should be promoted, considerable obstacles for its implementation are anticipated. Because of the long and difficult process of drug registration, pricing policies, relatively small market size and branded prescribing habits (World Bank, 1997).

Several initiatives have been seen as necessary to reform the pharmaceutical sector and achieve significant savings. Among these are the implementation of essential drug lists, introduction of treatment guidelines, promotion of generic prescribing, planning incentives to rationalise drug consumption, primarily through decentralisation of policies and granting more autonomy at facility level (WHO, 2003; World Bank, 1997).
Key Points on Jordan’s Health Infrastructure:

- The major health care providers in Jordan are the MOH, the private sector and the RMS. Smaller health care programmes are provided by the university and NGOs.

- Health expenditure is considerably high. The MOH and private sectors are the biggest in terms of expenditure and number of facilities. Almost 75% of hospital admissions take place in the private and the MOH hospitals.

- Hospital services and pharmaceuticals are the two most expensive components of health. Further increase in health spending is inevitable in the light of inefficient planning, overutilisation of hospital services, and lack of incentives for cost-containment, due to high centralisation of management, particularly in the public sector.

- Prevailing branded prescribing habits, excessive and irrational drug use, lack of treatment protocols, low enforcement of quality assurance measures, absence of drug use audit systems, particularly in secondary level care are all obstacles to rationalising pharmaceutical expenditure.

- Drug procurement policies in the public sector are resulting in drug shortages. In contrast to the private sector where drugs are usually available.

- The majority of manpower is in the private sector. Whereas, under-staffing is evident in the public sector due to lower income and fewer incentives.

- Generic prescribing, introduction of care standards and treatment guidelines, involving staff in decision-making, and improving work incentives are seen as major steps to curb costs and improve drug availability and use.
Commentary on the Literature Review:

The following are issues encountered during the literature review, which are perceived as noteworthy. As they were the main limitations encountered during the literature review, they are believed to be key areas to address to improve the quality of the literature published on Jordan.

1 - Substantial inconsistency exists in the reports on population demography and health conditions, even reports corresponding to the same year, e.g. the MOH and WHO reports. This introduces difficulty in interpreting data and adds to the ambiguity of the Jordanian health status.

2 - The reports obtained from the MOH were incomplete and sometimes inaccurate. This corroborated what has been published on the unreliability of health indicators calculated using the MOH reports.

3 - The results of the MOH disease surveillance systems were presented as tabulated numerals without analysis or discussion, which hindered their interpretation. For instance, variations in disease incidence rates across the different regions, population groups or time were unexplained. Consequently, identification of the causes of such variations was not possible. This would limit the value of these reports in planning health strategies.

4 - The ongoing research activity is limited and scattered, i.e. it does not pool into one national body through which research strategies could be informed and prioritised. This also endorses what has been recently published on importance of having a national strategy for research (WHO, 2003). Jordan is a fertile environment for health research with so many areas still unexplored. However, research prioritisation is imperative due to limited funding. Funds should be invested in the investigation of priority rather than auxiliary areas, as seen in several studies in Jordan. It is essential that research bodies collaborate to achieve this goal.

A spin-off from reviewing the literature on Jordan was providing the MOH archives with studies published in international journals, which were not locally available.
Health Conditions and Infrastructure:

The considerably high health expenditure and limited resources are primary challenges to the Jordanian health care system. Further increase in expenditure is foreseen with the increasing population, demographic shifting towards aging, and high prevalence of non-communicable diseases and their risk factors.

The ramifications of the unplanned capital investment in the private sector, whether hospitals or pharmacies, on the quality of service need to be addressed. From one perspective, it could increase the competition between providers, thus improve service quality or decrease charges. On the other hand, competition over a limited market size would decrease profit and result in cutting down the number or quality of services.

The ability to refer patients to more than one health program facilitates accessibility to care. However, in the light of lack of coordination among health care facilities, this might introduce imbalance in service utilisation leading to gaps, waste and duplication of health care services. Furthermore, it would undermine the continuity and appropriateness of care for patients referred across the different sectors.

In order to effectively plan public health education, people’s behaviours, beliefs, incentives, social, cultural and religious backgrounds should be taken into consideration. This is more challenging in a heterogenous society like that in Jordan. Especially that characteristics of the different population groups are under-investigated, due to the limited research.

Several gaps were identified in the literature. For example, the hospital systems; despite being the most expensive component of health spending, little is published on workflow within hospitals, hospital services’ utilisation, factors which influence medical practice, the role of different health care professionals and patient care at secondary level. Similarly, there is a paucity of information on prescribing practices, drug utilisation processes, their determinants and appropriateness, particularly at hospitals. Furthermore, the pharmacist role in patient care and rationalising drug use is not explored. Neither are
Chapter One

the views on clinical pharmacy practice and its introduction to Jordanian hospitals.

Implications of This Chapter:
The literature review has informed the planning of the project in terms of:
1- Area of investigation: Cardiac diseases were chosen as the area of investigation in this project. Since they are the leading cause of death and a primary cause of morbidity and hospitalisation, they are a priority area to investigate. They are also a key area for resource rationalisation and optimisation of disease management, especially that they are chronic, costly and have dramatic implications on patients’ lives. Reports on the excessive and irrational drug use, as well as the lack of information on drug utilisation patterns directed the project towards the evaluation of drug use in cardiac diseases.

2- The study settings: As hospitals are the most expensive component of care and they are considered by a majority of the population as the first point of contact for health services. Additionally, due to the paucity of information on patient care and drug utilisation at secondary care level in Jordan. Hospitals were chosen as the study setting.

In the light of the literature gaps listed above, and to enhance the understanding of patient care and drug use at hospitals, the project fieldwork proceeds with the exploration of these issues. This is through conducting interviews with key health care professionals in Jordan, with the aim of filling the gaps in the literature.

In the following chapter, the conduct of these interviews is presented along with the methods of selection and establishing accessibility to the study settings.
Chapter Two:

Interviewing Health Care Professionals in Jordan.

Introduction:
The previous chapter revealed how hospital care and pharmaceuticals were the two most expensive elements of health in Jordan. This directed the project to investigate the use of drugs at hospitals. The literature has reported overutilisation of the hospital services and irrational drug use. Unfortunately, it does not offer information on the patterns of drug utilisation, medical practice and patient care at secondary level. Furthermore, the pharmacist role in patient care is not identified. It was necessary to understand the workflow within hospitals, the factors which influence drug prescribing, and the role of pharmacists at hospitals, before proceeding with the evaluation of drug use. This chapter presents the results from the conduct of interviews with key health care professionals from different health sectors in Jordan, to explore the above issues and fill in the literature gaps. It also discusses the selection and accessibility to the hospitals, where the study fieldwork will be conducted.

Aim:
1- To establish the setting for the study fieldwork; interviews and drug use evaluation.
2- To fill in gaps in the literature in terms of drug utilisation, medical practice and patient care at secondary level.
3- To highlight the role of hospital pharmacists in patient care.

Objectives:
1- To choose and establish accessibility to the study hospitals.
2- To explore the study hospital settings, highlighting the following:
   a- Drug procurement policies, drug availability and factors affecting medical practice and drug utilisation processes.
   b- Role of medical team members in patient care, with focus on the role of hospital pharmacists. Also, the level and aspects of communication among health care professionals (HCPs) and their job limitations.
Chapter Two

c- Level and aspects of interaction between HCPs and patients, patient education and counselling services.

d- Drug information sources, continuing education activities and drug-related issues in need for further training for pharmacists, physicians, and nurses.

e- Perceptions and views of HCPs on the introduction of clinical pharmacy services to the MOH, university and private sectors.

3- To describe the experience of introducing clinical pharmacy practice into the RMS hospitals (army sector).

Methodology:
The project is a hospital-based one. For this purpose, the choice and accessibility to hospitals had to be established. This section describes the methods used to gain access to the study hospitals. Later, the methods of interviewing key HCPs in Jordan are presented.

1. Establishing the Setting for the Study Fieldwork:

1.1 Selection of the Study Hospitals:
A list of all hospitals in Jordan, illustrating their sectors and bed size was compiled. It served as a sampling frame to choose the study hospitals. Sampling was purposive where three major hospitals were chosen, a governmental (MOH), a university and a private hospital. The hospitals were selected because they are major referral hospitals that serve a majority of the population and cover a wide range of social classes. The MOH hospital is the major governmental hospital and the biggest of all hospitals in the country (MOH, 1999; MOH, 2004). This hospital was chosen since the head of the speciality department takes responsibility for the speciality in all other governmental hospitals across Jordan. The university hospital was chosen on the basis that it is the only hospital of this type at the time of sampling. Its inclusion in the sample will allow the exploration of drug use practices in one of the major teaching hospitals in the country. The hospital from the private sector was chosen to explore this quickly expanding sector, which accounts for more than 50% of total health expenditure and
around 79% of pharmaceutical expenditure (JFDA, 2003; JFDA, 2004; WHO, 2005). The abundance of resources in this sector, unlike the MOH and university sectors, will impart diversity to the findings and enrich the study. Furthermore, comparison between the three sectors will highlight the impact of resources on prescribing practice and drug utilisation. The private hospital was chosen because it is the biggest private hospital in Jordan (MOH, 2004). Besides, it has a teaching role, hence, the staff would be more receptive to the idea of conducting research, which would facilitate carrying out the study. Military hospitals were not investigated due to the strictness and confidentiality of the army sector, especially that the researcher has no military affiliations. Army permissions are requested for all activities, and they are lengthy and difficult to obtain. This was believed to hinder accessibility and the progress of the study. An example was the difficult and long wait experienced to obtain permission to conduct interviews with clinical pharmacists in the RMS hospitals. This setting only examine the role of hospital pharmacists.

1.2 Gaining Access to the Hospitals:
The head of each of the MOH, university and private hospitals were contacted to explain the aim of the project and seek permission to evaluate drug utilisation processes. Covering letters (appendix 1: A, B and C), the project protocol and the researcher’s curriculum vitae were submitted to the MOH and research committees at the three hospitals for evaluation. The university hospital requested a detailed covering letter in Arabic before granting its approval. This required translation and re-submission of letters. Eventually, approval to conduct the study in all hospitals was obtained.

In order to access the army hospitals to interview clinical pharmacists, the chief pharmacy manager was contacted for permission. The aim of the project and interview guide were discussed. However, the permission of the chairman of joint chiefs of staff was requested. A covering letter was prepared accordingly (appendix 1: D). It took three months to process paper work and obtain permission.
Chapter Two

2. Interviewing Key Health Care Professionals in Jordan:
The interviews were meant to complement the literature review -in chapter one- and fill in the gaps to provide an integral view on the health care system in Jordan.

2.1 Sampling and Recruitment:
The sample was a purposive one. Managers and senior HCPs from the MOH, university and private hospitals were targeted. This was due to their long work experience, hence, they were better candidates to describe the hospital system workflow and limitations. Junior staff were also included in the sample to explore their views on hospital systems, medical practice and drug utilisation. Some interviewees were recommended by their managers or colleagues, because they were prominent in their settings. For instance, the administrator of clinical pharmacy residency program at the RMS hospitals was recommended by the chief pharmacy manager. The sample included twenty two HCPs from different professions and sectors. These were as follows:

1- At university hospital: a senior administrative officer, a chief pharmacist, a pharmacist at an inpatient pharmacy, a cardiology consultant, a senior and a junior resident at the internal medicine department, a chief nurse and staff nurses at the CCU.
2- At MOH hospital: a chief pharmacist, a chief resident at the internal medicine department, a chief nurse and a staff-nurse at the CCU.
3- At private hospital: a chief resident, a cardiology resident, a chief pharmacist and a chief nurse.
4- At RMS hospital: the clinical pharmacy residency program administrator and a clinical pharmacy resident.

In addition to a senior officer at the Jordanian Pharmaceutical Association, a medical representative (MR), a senior consultant on health affairs at the MOH, and a senior officer at the Drug Department.

The clinical pharmacy program administrator at the RMS hospitals was contacted 2 years later for updated information on progress of the program.
2.2 Data Collection Tools and Procedures:

2.2.1 Interview Guides:
Comprehensive interview guides were prepared through reviewing the literature (appendix, 2). They comprised questions on health-related issues, which were lacking in the literature on Jordan. These included workflow in hospitals, role of medical team members and hospital pharmacists, factors which affect medical practice, prescribing habits, drug availability and use. In addition to use of therapy guidelines, therapy monitoring, communication among HCPs, continuing education activities for HCPs, drug information sources, HCPs-patient interaction, patient education and counselling. Moreover, the introduction and implementation of clinical pharmacy services, facilitators and challenges to the service. Several interview guides were prepared for the different HCPs from the university, MOH, private and army sectors. Open-ended questions were mainly used along with probes to allow in depth exploration of issues. The questions were revised and approved by the study supervisors. Later, they were translated into Arabic and revised by a supervisor in Jordan to verify the accuracy of translation.

2.2.2 Conduct of Interviews:
Interviewees were contacted in person or by telephone and the aim of the project was explained. Appointments to conduct interviews were arranged at the convenience of the interviewees. Twelve interviews were audio-tape recorded. The rest of interviews were hand-written because the interviewees did not feel comfortable about recording the interview or a tape-recorder was unavailable. The interviews lasted on average for an hour, ranging from 20 to 90 minutes. At the beginning of each interview, interviewees were reminded of the aim of the study and confidentiality was assured. Interviews were conducted in Arabic, in a face-to-face personal setting and at the interviewees' place of work. Only the interviews with the chief and staff nurses from the MOH hospital were conducted with both nurses present, because the interviews took place at the CCU. Although they were interviewed separately, interaction between them was inevitable.
The interviews were conducted in a loose semi-structured style to elaborate on as many issues as possible, given that they served the study objectives. Probing of interviewees occurred occasionally using non-leading questions. Sometimes, probing was directive, however, this was only when asking about factual data. Interruption occurred during most of the interviews due to busy work environments. Whenever this happened both the interrupted question and/or answer were repeated to remind the interviewee of the context. It is believed that interruption did not affect interviews, because most of the elicited information was factual and descriptive of work settings rather than personal feelings, which could be lost or withdrawn on interruption. Cessation of recording of interviews was requested by some interviewees when answering certain questions. On the other hand, some interviewees elaborated more on issues discussed during the interviews after stopping tape-recording at the end of the interviews. In both cases, answers were hand-written. Field notes on the researcher’s observations during interviews were also kept.

3. Analysis of Data:

3.1 Coding Data:
All interviews were transcribed in Arabic. Later, the data were simultaneously translated to English and coded by assigning it to different categories. The effect of translation on the validity of data was acknowledged. Hence, accuracy of translation to prevent change of content was sought as much as possible. Moreover, peers with bilingual skills (Arabic/English) and the supervisor in Jordan were consulted on some of the subsets of data. The categories for coding data were generated from the questions of the interview guides, as well as emerging themes; raised by the interviewees. Data were coded for the same question in all interviews before moving to the following question. The categories of data generated from each interview were listed, and similar categories across the interviews were marked to facilitate cross-referencing. Quotations and anecdotes stated by interviewees were sometimes used to present their views and opinions.
3.2 Content Analysis:

There is a wide variety of methods for the analysis of interview data (Miles and Huberman, 1994; Robson, 1993). Examples are:

- Matrices, such as, time-ordered, role-ordered, check-list, effects, case-dynamics and conceptually clustered matrices.
- Maps and plan diagrams.
- Networks and charts, such as causal networks, organisational, context and flow-charts.
- Case-studies, which study phenomena in their context, hence highlight the importance of contextual factors.

All of these methods force abstracting from a large amount of data, point out salient findings and/or the relationship between them. Hence, they facilitate interpreting data, noting patterns, and withdrawing conclusions.

Role-ordered matrices seemed particularly useful to perform content analysis of the interviews, because they allowed comparing views of the different HCPs, and brought data together in a way, which facilitated comparisons and cross-referencing. The matrices were manually prepared; with rows and columns representing the profession of interviewees and the coding categories, respectively (figure, 3). Views of interviewees from the same and different professions were compared within and across the different sectors. For example:

- views of physicians, nurses and pharmacists on the level of communication among them at each hospital.
- views of pharmacists from the three hospitals on drug procurement policies.
- views of physicians from the same or different hospitals on the introduction of therapy guidelines.

Data in the different categories were related, an example was relating the role of MR to the drug information sources used by HCPs. Furthermore, data were cross-referenced, which allowed its verification (triangulation), as views of different interviewees
regarding the same issues were compared. For instance, cross-referencing the views of physicians and pharmacists regarding pharmacists’ contribution to patient care. Flow charts were chosen to depict drug delivery systems at the three hospitals, because they present data in a concise, easy and sequential way, as depicted in figure 6, 7 and 8 (shown later in the section).

**Figure (3): Role-ordered Matrix:**

<table>
<thead>
<tr>
<th></th>
<th>Drug information sources</th>
<th>Drug procurement policies</th>
<th>Communication between HCPs</th>
<th>Continuing education activities</th>
<th>Role of hospital pharmacist</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physician</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nurses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medical Representative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results:

The Study Settings:
Approval was granted to conduct the study fieldwork at the three chosen hospitals, namely the MOH, university and private hospital. Also, the army permission to access the RMS hospital and interview clinical pharmacists was obtained.

Results From Interviewing Health Care Professionals in Jordan:

1. Response Rate:
All twenty two HCPs contacted agreed to be interviewed.

2. Themes Generated from the Interviews:
The interviews generated different themes, which were mainly related to drug availability and utilisation, medical practice and patient care at hospital settings. They also gave insight into the role of hospital pharmacists and views on clinical pharmacy practice. The themes were of two types: those addressed by the interview questions and ones raised by the interviewees (emerging themes). However, as both types overlap, they were presented together for simplicity and to give a coherent view of the study settings. The themes included:
- Drug procurement and supply.
- Factors which influence drug availability at hospitals.
- Medical team members and duties.
- Pharmacist-physician and pharmacist-nurse communication.
- Medical practice and the factors which influence prescribing and use of drugs.
- Therapy guidelines.
- Generic versus branded prescribing.
- Therapy monitoring and follow up of patients.
- Patient counselling services.
- Role of hospital pharmacists, and level of communication with patients.
- Views on the introduction of clinical pharmacy services to the study hospitals.
• Drug information sources, continuing education activities, and areas in need for training for pharmacists, nurses and physicians.

• The experience of clinical pharmacy practice in the army hospitals, highlighting the facilitators and challenges of introducing clinical pharmacy practice, its impact on physicians' practice, and pharmacists' input in patient care.

Under each of the above themes, data were presented in different sections representing the different hospitals or professions. This is to highlight differences across the study settings or the perspectives of different HCPs.

2.1 Drug Procurement and Supply:
Drug procurement in both the MOH and university hospital occurs through tenders, which provide drugs in bulk at lowest prices. Every year the MOH and university invite for tenders to provide an approved list of drugs. The list is annually updated and includes estimates of drug quantities needed the year depending on drug consumption in the previous year and including a percentage of annual increase in consumption. Inviting tenders takes place announcing the drug generic names, specifications and quantities. Tenders settle on suppliers who fulfill the required specifications at lowest prices. At the MOH hospital drugs are delivered from central MOH stores upon the submission of supply orders. Whereas at the university hospital drugs are directly delivered from the suppliers. In both hospitals, if a drug or its alternatives are unavailable, the drug is purchased from the private sector. However, this is only for civil employees and their dependants at the MOH hospital. As for the university hospital, patients bear drug costs either entirely or partially depending on their insurance status.

In contrast to the above two hospitals, drug procurement in the private hospital takes place through bulk purchase. All drugs prescribed by physicians, whether generic or branded were reported by the chief pharmacist to be provided, regardless the costs. However, because many of the physicians were reported to hold shares at the hospital, they cooperate with the pharmacy to curb drug costs, by prescribing brands from suppliers who offer better prices and services.
2.2 *Factors Which Influence Drug Availability at Hospitals:*

The private hospital was reported to have most of the drugs available in the market. Unlike the case at the MOH and university hospitals, where the chief pharmacists stated encountering serious drug shortages as a result of the limited resources and the drug procurement policies (table, 4). Drug shortages in the private hospital were stated to occur for reasons out of the hospital control (table, 4). These were also reported at the other two hospitals. Examples of these reasons were waiting for the Jordan FDA approval to release drugs into the market, which was usually a lengthy and complex process, or the dispute between the authorities and drug suppliers on drug pricing, hence the drug importation ceased.

As shown in table (4) hospital-related reasons of drug shortages were exclusively evident at the MOH and the university hospitals. One of the reasons reported at the university hospital was the irrational and excessive use of medication. The chief pharmacist stated that physicians tended to write prescriptions for larger doses than what was actually prescribed, e.g. they wrote a prescription for a twice daily dose although the actually prescribed dose was once daily. Hence, the patients were dispensed double the quantity of medication, so that they would not need to visit the hospital pharmacy more than once. This resulted in quick consumption of stock and inability to meet the needs of all patients.

Both chief pharmacists at the MOH and university hospitals stated that although drug alternatives existed, patients’ satisfaction was affected when the prescribed brand was not dispensed.
### Table (4): Reasons of Drug Shortage at the Study Hospitals:

<table>
<thead>
<tr>
<th>Reasons of Drug Shortage</th>
<th>MOH</th>
<th>University</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Out of hospital control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1- Drugs were awaiting approval of the Jordan FDA to be released to the market.</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>2- Drugs were not imported by drug suppliers.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3- Physicians prescribed unregistered drugs which were unavailable at market.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Under hospital control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1- Limited resources.</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>2- Delays in inviting or settling on drug tenders.</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>3- Under-estimation of annual drug needs.</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>4- Arbitrary, irrational and excessive drug use.</td>
<td>NR*</td>
<td>✓</td>
<td>NR*</td>
</tr>
</tbody>
</table>

* NR: Not reported by interviewees.

### 2.3 Medical Team Rounds, Members and Duties:

In all the hospitals medical rounds were reported to take place on daily basis; a morning and an evening round. The rounds were attended primarily by consultants and medical residents. Nurses were reported to participate in the rounds at the MOH and private hospitals, but not at the university hospital. While the senior resident at the MOH hospital stated that nurses’ participation occurred upon physicians’ request. The chief and staff nurses at the CCU stated participating freely in the rounds. However, they stated that it depended on the type of ward (medical vs CCU) and working shift (morning vs evening). Pharmacists did not take part in medical rounds at any of the hospitals. Until very recently that a non-specialised pharmacist started attending the rounds in the MOH hospital only. However, this was described as sporadic and on irregular basis. Medical and/or pharmacy students also participated in rounds at the MOH and university hospital. Whereas at the private hospital students existed only if the hospital had a teaching role. Duties reported to take place in a medical round were similar across the different hospitals. They included physical examination of patients, decisions on diagnosis, management and drug therapy, therapy monitoring, patients
follow up, and teaching residents and students. The number of patients seen during a medical round varied with the type of speciality at the three hospitals. For instance, the university resident stated seeing -on most of the days- at least 7-10 patients per round, which might exceed 30 patients in some specialities. Similarly, the MOH resident stated that number of patients per round ranges from 1-2 patients in some specialities up to 20-25 patients in other specialities. In addition to the variation by speciality, the senior resident at the private hospital stated seasonal variation in the number of cardiac patients. More patients were admitted in summer than in winter, ranging between 15-20 and 7-8 patients per round. The average time spent with each patient was almost similar at the three hospitals. Physicians’ estimation of the time ranged between 3-5 minutes at the university hospital and 5-10 minutes at the MOH and private hospitals. Longer periods up to a maximum of 15 minutes were reported, yet the MOH physician stated that this was usually with critically ill patients. Physician-patient interaction was reported to take place at the three hospitals. However, it was stated not to always occur at the university and the MOH hospitals. Interaction involved discussing with patients their health condition, and in the private hospital patient education was reported. The university physician stated that interaction with patients was mainly done by residents and not consultants. It was described as brief, and believed to occur as an inevitable result of approaching the patients’ beds, rather than the wish to involve patients in the care process.

2.4 Pharmacist-Physician and Pharmacist-Nurse Communication:

The University Hospital:

Poor coordination between HCPs as well as hospital departments was reported. In order to improve communication among HCPs and enhance medical practice, the physician emphasised the importance of leadership of the medical team and suggested giving it to physicians, who shall steer the efforts of the team members.

A conflict in the reports of pharmacists and physicians regarding their level of communication was noted. One physician stated that communication occurred only sometimes, concerning drug information not found in physicians’ references, e.g. drug
indications or side effects. Drug dosing was described as a rarely enquired about subject, because of the pharmacists' limited clinical experience. Additionally, pharmacists were reported not to refer to clinical trials, which were considered a primary source of evidence-based information on dosing. In contrast, the chief pharmacist reported an extensive level of communication between pharmacists and physicians in the outpatient and inpatient pharmacies, which involved enquiring about drug-related issues, such as drug availability, alternatives, use and dosing. Another pharmacist at one of the inpatient pharmacies stated that physicians contacted pharmacists mainly to enquire about generic drug names, dosing and dose adjustment in renal failure. While pharmacists contacted physicians if the medication chart was illegible or dosing errors were detected. The pharmacist added that drug enquiries were frequently received from junior physicians, while none from consultants. Conversely, a junior physician asserted communication with pharmacists at a minimal level, mainly regarding drug availability and not pharmacology, dosing or drug interactions.

Pharmacist-nurse interaction was described by the inpatient pharmacist as limited, mainly to assess nurses in reading the drug package insert or to answer questions on new drugs.

The Private Hospital:
Pharmacist-physician communication was described by the physician as irregular, taking place when physicians wished to obtain drug information leaflets from the pharmacy or enquired about drug dosing, dose timing, or generic names. Pharmacists, on the other hand, contacted physicians if a prescription was unclear or the drug was unavailable. This corroborated the chief pharmacist's reports on communicating with physicians regarding drug dosing, availability, alternatives and generic names. Pharmacist-nurse communication occurred during supplying wards with medication, also when explaining drug administration methods.

The MOH Hospital:
Similar to the university hospital, conflicting reports of the MOH physician and
pharmacist regarding their communication were noticed. The chief resident described it as very rare, while the chief pharmacist stated that physicians enquired about drugs, doses and drug alternatives.

Pharmacist-nurse interaction was reported, by the pharmacist, to occur during supplying wards with medication. However, the CCU chief nurse stated asking pharmacists about new drugs, doses, side effects and generic names. This, however, took place only during nurses’ morning shifts, because no pharmacists were available in the evening. Generally, the chief and staff nurses reported a good level of communication among HCPs in the CCU, because of the small number of patients and less workload. While communication was absent on medical wards due to the high workload and inadequate staff (1 nurse /11-12 patients).

**2.5 Medical Practice and Factors which Influence Prescribing and Choice of Drugs:**
An array of overlapping factors were reported to affect medical practice and the choice of drugs at the three hospitals. These were as follows:

**2.5.1 Type of Sector:**
The physician at the university hospital stated that the type of sector largely influenced medical practice (figure, 4). A considerable level of medical practice at the governmental hospitals was believed not to rely on sound clinical evidence. This was attributed to the seriously limited resources, high workload and lack of equipment, rather than inadequate knowledge of HCPs. Inappropriate medical practice was expected in private hospitals too, however, ascribed to different reasons. It was claimed that physicians at private hospitals tend to order unnecessary medical procedures to increase their profit.

Conversely, medical practice at the university and army hospitals was described as more neutral than in the private and MOH sectors. Because resources were not as limited as in the MOH sector. Also, physicians were salaried rather than being share holders, thus they were not tempted to increase their profit as in the private sector. Nonetheless, the
physician reported high workload and under-staffing in nursing at the university hospital, which was impeding medical practice.

The reports of the university physician on practice at the governmental hospitals were affirmed by the MOH physician, who stated limited resources and unavailability of drugs, medical equipment, and laboratory kits. The physician elaborated that when drugs were unavailable at the MOH hospital and could not be purchased from the private sector, alternatives were prescribed even if less appropriate. Furthermore, laboratory services were described as inefficient and delayed. The physician mentioned that sometimes patients stayed at hospital for 2-4 weeks due to the lack of diagnostic tools. When tests could not be done at the hospital, patients were referred to private laboratories. However, most of the MOH patients were reportedly from a humble socio-economic class, who could not afford private laboratory fees. Hence, the tests were not done. Other factors which impeded medical practice at the MOH hospital were the delay in nursing services and the long waiting times for patients' referral for consultation. All of these factors were stated to hinder prompt and effective health care and increased length of hospital stay (LOS). The MOH physician expressed feeling exhausted and stressed by all of these limitations.

Conversely, the physician in the private hospital could not recall any limitations to his practice. The physician explained that resources were available, facilities were well-equipped, workload was not high, staffing was adequate, nursing services were prompt, laboratory tests were quickly performed as well as patients' referral for consultation. Furthermore, most drugs were available. Also, having the hospital system computerised further facilitated accessing patient data. This was believed to enable physicians to focus on patient care, rather than being overloaded with nurses tasks as the situation was at the MOH hospital. However, the physician pointed out how expensive private medical care was, which could not be afforded by all citizens, thus they used the MOH hospitals.
2.5.2 Type of Hospital:

The type of hospital was stated as one of the factors, which affect medical practice (figure, 4). In the university hospital, medical practice was described as up-to-date and evidence-based. This was believed to be enhanced by the role of hospital as a major teaching institute. Nevertheless, defects were believed to exist in patient care and service delivery. One physician stated that they treated diseases without addressing social and psychological aspects of care or disease implications on patients’ lives.

Consultants, mainly the younger generations, were described as distant from patients, because they depended mostly on clinical investigations to diagnose diseases, while residents carried out physical examination of patients. On the contrary, veteran consultants were stated to thoroughly examine patients, which was believed to affect patients’ satisfaction with medical practice as they felt better cared for by physicians.

Medical practice at the university and private hospitals was described as more specialised than at the MOH hospital. This was attributed to the specialisation programs run at the two former hospitals. Specialisation was believed to enhance patient care, as it eliminated the need to refer patients to speciality units and endure delays as in the MOH hospital.

2.5.3 The Hospital Administration Policy:

In the university hospital, the senior resident believed that lack of resources and drug unavailability partially resulted from the hospital management policies. Lack of

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**Figure (4): Factors which Influence Medical Practice.**

- Type of health sector, type of hospital and availability of resources.
- Medical schools and consultants’ practice.
- Hospital administration policy.
- Incentives, income, and workload.
- Drug procurement policies and drug availability.
- Communication among HCPs.
- Lack of treatment protocols and standardisation of practice.
- Patient education, compliance, and feedback on medication.
- MRs and pharmaceutical promotion.
prioritisation, mis-allocation and non-rationalisation of resources were stated. The resident reported that sometimes the hospital provided only one member of a therapeutic group, e.g. one member of the ACE-Inhibitors family, because it dealt with only one company. Although other companies had other agents. This forced physicians to prescribe the available drug even if it was not the treatment of choice. Furthermore, it was claimed that the dispute between management personnel affected the decisions on allocation of medication to the different hospital wards. The physician proposed decentralisation of decision making to a departmental level, and anticipated that it would enhance staff involvement in their systems and motivates them to rationalise resources.

At the MOH hospital, the physician stated that hospital management interfered mildly with their practice. Yet, it exerted pressure on physicians to treat patients at the hospital rather than referring them to other sectors, also to minimise patient hospitalisation periods. In contrast, the physician from the private hospital reported that the hospital administration did not interfere with their practice.

2.5.4 Medical Schools and Consultants’ Practice:
In the private hospital, medical practice was described as diverse even when treating similar conditions, e.g. the diversity in prescribing antihypertensive medication. Diversity was ascribed to the fact that consultants were trained at different medical schools, predominantly American medical schools, followed by British schools. Nonetheless, the interviewee argued that the diversity in treating similar condition was minor and complied with established disease management protocols. Similar reports were given by the university hospital physician, who stated diversity in prescribing practice, and asserted that the choice of drug therapy was highly influenced by consultants’ practice (table, 5). Practice primarily followed American and British medical schools.

2.5.5 Pharmaceutical Promotion and Medical Representatives (MRs):
The chief pharmacist in the private hospital pointed out the influence of MRs on prescribing practice (figure, 4). A decline in prescribing some drug brands was noticed
when the MR promoting them stopped visiting physicians. The MOH physician believed that prescribing habits could be easily changed. Similarly the physician at the private hospital stated that changing prescribing habits could be achieved if scientific evidence was provided on more benefits, less side effects or better patient tolerance with alternative prescribing practice. However, an MR classified physicians into veterans, whose prescribing habits were difficult to change due to their long experience with old drugs, and young physicians who were more receptive to new drugs.

Table (5): Factors Perceived to Influence the Choice of Drug Therapy:

<table>
<thead>
<tr>
<th>Factors which Influence Choice of Drugs Therapy</th>
<th>MOH</th>
<th>University</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Appropriateness of therapy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Therapy outcome.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Drug availability.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4. Drug cost.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Patient response to therapy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physician factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Experience with drugs.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Drug factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Drug availability.</td>
<td></td>
<td></td>
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<tr>
<td>2. Drug cost.</td>
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<td></td>
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<tr>
<td><strong>Patient factor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Patient compliance.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. Patient educational level.</td>
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<td></td>
</tr>
<tr>
<td><strong>Physician factor:</strong></td>
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<td></td>
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</tbody>
</table>

2.5.6 Job Incentives and Workload:

Job incentives for physicians at the MOH and the university hospitals were described as few due to low salaries and high workload. Unlike the situation in the private sector where income was higher and workload was less. The MOH physician reported that
unlike the situation in the MOH hospital, both patients and physicians in the private sector were satisfied. The former with the service provided and the latter with the job and income. To overcome job limitations at the MOH sector (table, 6), the physician stressed on having more funds. However, pessimism was expressed regarding rectifying the current situation and improving job conditions.

The senior resident at the university hospital felt he was not fairly rewarded, also not supported by the hospital administration. He ascribed this to lack of incentive, relatively low income and high workload, which was believed to negatively affect physicians’ motivation for work and suppressed their sense of belonging to their settings.

Besides their tasks the physicians stated doing some nursing tasks. For instance, transferring patients between departments, withdrawing blood samples, delivering samples to and from the laboratory if they were urgent.

The physician at the university hospital added that they also served the patients’ families due to the unavailability of social workers (table, 6). It was described as time consuming and very distracting. The physician suggested devolving some of these tasks onto nurses and technicians to decrease their workload.
### Table (6): Job Limitations for Pharmacists, Physicians and Nurses in all Hospitals:

| Pharmacists | • Work is done manually because systems are not computerised, which is very time consuming and leads to high workload. (MOH and university hospitals)  
| • Inadequate number of pharmacists. (MOH and university hospitals)  
| • Drug unavailability. (MOH and university hospitals)  
| • Lack of treatment protocols. (all hospitals)  
| • Non-cooperation of physicians to prescribe alternatives when certain brands are unavailable, resulting in patients dissatisfaction. (private hospital)  
| • Lack of continuing education activities. (all hospitals)  
| • Drug companies not viewing pharmacists as an important target as physicians for drug promotion, which leaves pharmacists behind in terms of knowledge on new drugs in market and drug availability. (private hospital) |
| Physicians | • High workload due to high patient demand and inadequate staff. (MOH and university hospitals)  
| • Low income and inadequate incentives. (MOH and university hospitals)  
| • Lack of cooperation between different HCPs.  
| • Lack of social workers to care for patients and their families. (all hospitals)  
| • Inadequate information sources, which allow neutral assessment of drugs. |
| Nurses | • High workload, under-staffing, low incentives, and unavailability of equipment. (MOH and university hospitals) |

Overhauling and maintenance of medical equipment: The CCU nurse at the MOH hospital stated shortages in equipment such as monitors, respirators, pump machines and flow rate devices. The available equipment were described as very old and not operating properly. Furthermore, technical maintenance of these equipment is absent. This was reported to impede drug administration and therapy monitoring.
2.5.7 Patient Education, Compliance and Feedback on Medication:

University Hospital:
Patient compliance was reported by the university physician to largely affect the choice of therapy (table, 5). Patients’ level of education was believed to determine their compliance to medical orders and demand for drug information. The interviewee stated that educated patients were more likely to contact doctors and ask questions about their medication than less educated patients. Most of the patients at the university hospital were reported to come from a low socio-economic class and many of them were illiterate or of little education, which was perceived to hinder patient care. An example was given on patients’ re-admission to hospital with atrial fibrillation as a result of abrupt cessation of beta-blockers. This was attributed to either the patients’ non-compliance to therapy, or to running out of medication without referring to the doctor for a refill prescription. To enhance patients compliance to therapy, especially elderly, doctors were reported to prescribe drugs of less dosing frequency. Furthermore, to prevent drug discontinuation, physicians gave patients an extra refill prescription so that they could obtain drugs from pharmacy without having to re-visit the clinic and endure long waiting times to get refill prescriptions.

Lack of patient feedback on medication was believed to affect medical practice (figure, 4). The physician elaborated that patients -during follow up visits- did not usually mention their experiences with taking the medication, e.g. side effects such as cough with ACE-inhibitors. As a result, the physician stated not being able to identify treatment strategies which were most effective, i.e. the goal of therapy could be achieved without knowing if the method used was the most appropriate or not. Again, this was attributed to illiteracy or low educational level of most of the patients, which was perceived to hinder the assessment of practice outcome.

The MOH Hospital:
The MOH physician did not consider patient compliance a primary factor when choosing drug therapy. Alternatively, appropriateness of therapy, therapy outcome, patient response, drug cost, availability, and physicians’ experience with drugs were
listed as determinants of the choice of drugs (table, 5).

The Private Hospital:
The physician from the private hospital elaborated that the choice of drugs relied on therapy appropriateness, concomitant therapy, side effects, contraindications, patient response, compliance and preference (table, 5). It was stated that some patients mainly the elderly preferred to continue taking the same drug brand. As a result the physician continued prescribing this brand even if alternatives existed, because it was believed to maintain patients' satisfaction with therapy. Patient benefit was believed to outweigh drug cost.

2.6 Therapy Guidelines:
The absence of therapy guidelines or hospital formularies was reported in all the study hospitals. One exception was at the MOH hospital, where the senior resident stated having guidelines for a few diseases such as ischemic heart diseases or for the use of chemotherapy. The physicians' views on the introduction of guidelines were divided into opponents and advocates. The opponents believed that guidelines would not enhance medical practice. This was ascribed to the fact that guidelines were general and insensitive to inter-patient variability. Hence, they were perceived inadequate to guide practice. Furthermore, the physicians at the private and the university hospitals stated that physicians' knowledge on disease management was satisfactory, which eliminated the need for guidelines. Alternatively, the physicians suggested the introduction of guidelines on the use and monitoring of medication. The cardiologist at the university hospital advised on conducting research on drug utilisation processes or the communication among HCPs and its impact on drug use.

Advocates, on the other hand, stated that the absence of guidelines resulted in the inappropriate use of medication and influenced physicians' confidence in practice. The physician at the university hospital explained that the lack of practice standardisation exposed the physicians to medico-legal liability, if inappropriate interventions were used. The introduction of guidelines was believed to render practice safer and boost
physicians’ confidence. Addressing inter-patient variability and tailoring therapy to specific patient needs were stressed.

2.7 Generic Versus Branded Prescribing:
In both the MOH and private hospitals, physicians and pharmacists reported that branded prescribing was the prevailing practice. While at the university hospital, generic prescribing was reported for educational purposes. However, both the resident and the chief pharmacist at the university agreed that physicians’ practices were inconsistent; mixing generic and branded prescribing. When asked about the reason of his generic prescribing practice, the university resident gave a negative answer (he did not know).

Regardless of the prescribing practice, pharmacists at the MOH and university hospitals stated referring to generic rather than branded drug names when dispensing medication, because drug brands were not always available. Conversely, the private hospital pharmacist provided all drugs, whether brands or generic.

2.8 Monitoring Therapy and Follow-Up of Patients:
All the physicians and pharmacists at the three hospitals stated that therapy monitoring and follow-up of patients were exclusively done by physicians. Physicians at the three hospitals reported daily follow up of patients during medical rounds, which involved therapy monitoring and assessment of patient response. Only the chief pharmacist at the university hospital mentioned that pharmacists might have a role in monitoring therapy. However, this was not endorsed by any evidence during data analysis.

2.9 Patient Counselling Services:
The University Hospital:
Counselling services for inpatients were reported to be exclusively done by physicians only on discharge. Counselling focussed on medication, which merely involved informing patients that a prescription had been issued for them and to be collected from the outpatient pharmacy, without discussing the use of medication. However, psychological and social implications of the diseases on patients’ lives were not
addressed. The resident reported that many diabetic patients left the hospital with well controlled blood sugar levels, but inadequate knowledge of diabetes, its complications, and the social implications of the disease on their lives. Another example was given of patients’ re-admission to hospital as a result of wrong use of drugs, such as abrupt cessation of beta-blocker therapy which resulted in patients’ readmission due to suffering withdrawal symptoms. This was attributed to not cautioning patients against sudden cessation of therapy. Similarly, emergency admissions of many bronchial asthma patients, who were found using inhaler devices erroneously. The physician explained that patients were only verbally instructed on using inhalers without having a demonstration or being supervised.

The Private Hospital:
Similar to the university, patient counselling was done by physicians on discharge. However, it involved detailed instructions on medication.

The MOH Hospital:
Unlike the above two sectors, patient education was done by nurses on discharge, as well as pharmacists when dispensing discharge medication from the outpatient pharmacy, a senior resident reported. The chief nurse in CCU stated answering patients’ questions on medication during their hospital stay and on discharge. Furthermore, nurses advise patients on diet, exercise, and smoking cessation. However, this was only for patients in CCU and not medical wards, where communication with patients was hindered by high workload and inadequate staff.

The senior resident stressed on the importance of patient education and counselling services. Simultaneously, he emphasised that patients should respect and comply to medical orders. The resident also believed that medical advice should not be ample, as it would overwhelm and confuse the patients, and lead to misunderstanding or false assumptions, which might impede physician-patient communication.
Chapter Two

2.10 Role of Hospital Pharmacists and Pharmacist-Patient Interaction:
Pharmacist in all hospitals reported that the role of hospital pharmacists was mainly concerned with drug procurement, supply, storage, inventory and dispensing (figure, 5). Tasks like preparation of drug supply orders, monitoring stock expiry dates, dispensing and instructing patients on drug use were done by outpatient pharmacists. They also checked doses and contacted physicians in case of wrong or over-dosing. Pharmacists in inpatient pharmacies prepared medication according to the medication charts, calculated costs of medication used by inpatients, and sent it to the accounting department. There was no interaction between pharmacists and inpatients, except in the university hospital where pharmacists interacted with patients only on discharge to dispense discharge medication (figures 6, 7, 8). Interaction was greater with outpatients, as it involved advising patients and answering their queries on medication. In both the university and MOH hospitals communication between pharmacists and outpatients was described as moderate, while thorough at the private hospital. The restrictions on drug quantities dispensed to outpatients in the two former hospitals, further reflected the limited drug availability at these hospitals, unlike the situation in the private hospital where no restrictions were enforced on dispensed drug quantities (figures 6, 7, 8).

The pharmacists were more involved in drug distribution systems at the private hospital, whereas at the university and MOH hospitals, nurses handled the processing of drug orders until administration to patients (figure 6, 7, 8). Pharmacist in the university and MOH hospitals carried out drug preparation on a very limited scale, such as eye drops and topical preparations. This role did not exist for pharmacists in the private hospital. In all hospitals, intravenous (iv) preparations and chemotherapy were entirely handled by nurses, except in the university hospital where a chemotherapy pharmacist prepared cytotoxic drugs.

Clinical pharmacy services were unavailable and pharmacists were not part of the medical round in all hospitals. Only in the army sector, and very recently at the MOH hospital that clinical pharmacy practice was introduced. This is further discussed below.
Pharmacists at the three hospitals expressed their wish to have a more active role in patient care beyond dispensing medication. However, they stated being hindered by several job limitations (table, 6). These were:

1- At the MOH and university hospitals: Clerical duties such as performing inventory and monitoring drug stock, which were done manually because the systems were not computerised. These were described as cumbersome and very time consuming. The chief pharmacist at the university hospital reported being in the process of installing computer systems.

2- At the private and the university hospitals: The insufficient numbers of staff, which was placing a high workload on the existing pharmacists.

Figure (5): Role of Hospital Pharmacists:

- Drug procurement, storage, inventory and monitoring stock.
- Drug distribution to different hospital departments.
- Dispensing medication to outpatients and inpatients.
- Instructing patients on drug use on discharge and in outpatient settings.
- Preparation of eye drops*, topical preparations*, and chemotherapy.*
- Answering HCPs queries on medication.
- Participating in medical rounds (only recently at the MOH hospital and on irregular basis).

* At MOH and university hospitals only. † At university hospital only.
Figure (6): Drug Distribution System at the MOH Hospital:

A) In-patients:
- Physicians write drug orders
- Nurses transcribe the prescribed drugs into special forms
- Forms are signed by:
  - nurse
  - head nurse
  - physician
- Ward pharmacy
- Drugs are dispensed in a 24 hour supply (no unit dose system)
- Nurses deliver drugs to ward
- Nurses administer drugs to patients

Occasionally pharmacists go up to the ward and verify medication forms against physicians' orders

B) Out-patients:
- Outpatient prescription
- Outpatient Pharmacy
- Drugs are dispensed for a one month supply (except antibiotics, for which a 5-day supply is dispensed, unless otherwise indicated by the physician)
Figure (7): Drug Distribution System at the University Hospital:

A) In-patients:

1. Physicians write drug orders
2. Nurses transcribe the prescribed drugs into medication sheet
3. Ward pharmacy
4. Drugs are dispensed for 24 hours (doses for each patient are placed in a compartment in a trolley) (unit dose system)
5. Nurses double check drugs against the medication sheet
6. Nurses deliver drugs to ward
7. Nurses administer drugs to patients

Upon discharge:

- In-patients with a discharge prescription
- Drugs are dispensed in doses enough to cover till the next follow-up visit

B) Out-patients:

1. Patients referred from Out-patient clinics with prescriptions
2. Out-patient pharmacy
3. Drugs are dispensed for a one month supply

Patients with refill prescriptions (usually receive 3 prescriptions for 3 months)
Figure (8): Drug Distribution System at the Private Hospital:

A) In-patients:

- Pharmacists in central inpatient pharmacy go to wards
- Transcribe the prescribed drugs into special forms along with head nurses
- Take forms to pharmacy
- Drugs are dispensed for 24 hours (unit dose system)
- Pharmacists deliver drugs to ward and place doses for each patient in a compartment in a trolley
- Nurses administer drugs to patients

B) Out-patients:

- Patients referred from outpatient clinics
- Patients coming on their own
- Inpatients with discharge prescriptions
- Outpatient pharmacy
- Dispense drugs as prescribed

Nurses come to pharmacy and take drugs to wards (in small wards).
Chapter Two

2.11 Views on the Introduction of Clinical Pharmacy Services:
All interviewees were familiar with the concept of clinical pharmacy practice from international settings. The idea of introducing clinical pharmacy services was welcomed by all physicians and pharmacists in the three hospitals. Pharmacists believed that having clinical pharmacy services would rationalise drug use, minimise waste and prevent medication errors. Furthermore, clinical pharmacists would provide drug information to HCPs, assist in drug therapy decisions, and decrease workload on present pharmacists. Similarly, physicians believed in the necessity of implementing clinical pharmacy services, particularly provision of drug information to physicians and patients. Pharmacists were perceived -by physicians- as the best candidates to educate patients on medication, hence increase compliance to therapy. The majority of interviewees thought the implementation of clinical pharmacy services was possible in their hospitals. However, the chief pharmacist at the private hospital asserted the necessity of having well-trained clinical pharmacists, especially that opposition by some physicians to this new role of pharmacists was anticipated. The introduction of incompetent clinical pharmacists was foreseen to minimise the expected benefits from service, and might lead to negative results. Failure of the experience at an early stage would jeopardise its continuation or introduction to other hospitals.

2.12 Drug Information Sources:

a- Pharmacists:
Several drug information sources were listed by the pharmacists at the three hospitals (table, 7). Medical representatives (MRs) were described by the chief pharmacists in all the hospitals as an important source of drug information, cost, availability at suppliers and new drugs in the market. MRs visited chief pharmacists only, and supplied them with drug brochures, leaflets, clinical studies and invited them to lectures and seminars. Both chief pharmacists at the university and the MOH hospitals described the information given by the MRs as scientific, yet, asserted its promotional nature. The university pharmacist added that such information could be misleading.
Drug information sources used by pharmacists also included the British National Formulary (BNF, published jointly by the BMJ Publishing Group Ltd and the Royal Pharmaceutical Society of Great Britain, with continual updates), the Martindale (published with continual updates by the Royal Pharmaceutical Society of Great Britain), the MEMI (published with continual updates by CCM Group) and Drug Indexes (unspecified).

b- Physicians:
In all the hospitals, the physicians stated depending on the available medical references and drug package leaflets for drug information (table, 7). The Harrison Manual of Medicine (published with continual updates by McGraw-Hill Companies, Inc), The Washington Manual (published with continual updates by Lippincott Williams & Wilkins) and the Martindale were the references mostly used at the university hospital. Whereas the MEMI, medical and clinical pharmacology books were listed at the physician at private hospital. Referral to pharmacists for drug information was reported only at the university hospital by one senior resident, but not the consultant. Conversely, MRs were considered a primary source of drug information for physicians in all hospitals. They invited physicians to lectures and seminars on drugs, also supplied them with drug samples, brochures, and clinical studies. The resident in the private hospital indicated the promotional nature of the information offered by MR. Likewise, the senior resident at the university hospital described drug promotion campaigns as misleading, because they portrayed new drugs as “magic drugs”, and did not present information that allowed neutral assessment of drugs.

c- Nurses:
The chief nurse in the private hospital reported that nurses relied on their university education and continuing education activities. Furthermore, they referred to physicians, pharmacists and drug leaflets for information on new drugs. Similarly, the chief nurse at the MOH hospital stated that nurses depended, for information on drugs, on pharmacists, physicians, lectures given by MRs, and drug formularies, predominantly, the MEMI. In contrast, the MOH staff nurse denied referring to pharmacists for drug
information. Instead, peer nurses, physicians and the MEMI were sought for information. In the university hospital, the chief nurse reported depending on continuing education activities for information on drugs. She did not include pharmacists in the sources of drug information. Nurses’ drug information sources are listed in table (7).

Table (7): Drug Information Sources Reported by HCPs at the Three Hospitals:

<table>
<thead>
<tr>
<th>Pharmacists</th>
<th>Physicians</th>
<th>Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- MEMI, Martindale, MEPO, BNF, and Drug Indexes. 2- Drug information leaflets. 3- Lectures and seminars by drug companies, especially on new drugs. 4- Promotional materials provided by MRs.</td>
<td>1- Medical and pharmacology references. 2- Drug information leaflets. 3- Martindale, MEMI, and The Harrison &amp; Washington Manuals. 4- Clinical trials. 5- MRs: drug samples, brochures, leaflets, clinical studies and lectures. 6- Pharmacists.</td>
<td>1- University education. 2- Continuing education activities. 3- Drug information leaflets. 4- Physicians, pharmacists, and peer nurses. 5- MEMI. 6- Lectures by MRs on new drugs.</td>
</tr>
</tbody>
</table>

2.13 Continuing Education for Pharmacists, Physicians and Nurses:

Among the three professions, pharmacists were the least likely to participate in continuing education activities at the three hospitals (table, 8). Continuing education activities for each profession are presented below.

Pharmacists:
Pharmacists in the MOH and private hospitals reported absence of continuing education activities. In contrast, the chief pharmacist at the university hospital mentioned having lectures once or twice a month, especially when new drugs were introduced. However, other evidence did not endorse the chief pharmacist’s statements. A pharmacist at the same hospital asserted that there were no educational activities in the hospital, except
for lectures organised by drug companies. These were described as infrequent, irregular
and usually discussed new drugs. Additionally, they had a scientific content but a
promotional nature, and focused on drug indications and benefits, while side effects, or
contraindications were not always presented.

Physicians:
Regular daily and weekly educational activities were reported by physicians at the
university and private hospitals. They provided up-to-date information on disease
management and drug use, and involved submitting daily patient reports, lectures and
seminars. Conversely, the chief resident at the MOH hospital confirmed that there were
no educational activities held during the past six months - from interview time - except
for presenting daily reports on patients to consultants during medical rounds (table, 8).

Nurses:
Chief nurses at the three hospitals reported having continuing education activities, such
as lectures, seminars and training courses (table, 8). In the private hospital lectures were
given monthly on a variety of topics such as infection control, chemotherapy, care for
pregnant women or families of deceasing patients. In the university hospital educational
activities were run by nurses, which involved new drug policies, disease management,
medical procedures, and gaps in patient care, such as inappropriate drug administration.
At the MOH hospital, continuing education activities were regularly run by a unit for
nursing development and education. Additionally, nurses reported attending lectures
given by MR on new drugs.
Table (8): Continuing Education Activities for HCPs at the Three Hospitals:

<table>
<thead>
<tr>
<th></th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists</td>
<td>Lectures and seminars (irregular, frequency undetermined).</td>
<td>None.</td>
<td>None.</td>
</tr>
<tr>
<td>Physicians</td>
<td>Daily reports - Lectures and seminars on daily and weekly basis.</td>
<td>Daily reports.</td>
<td>Daily reports - Lectures and seminars on daily and weekly basis.</td>
</tr>
<tr>
<td>Nurses</td>
<td>Lectures - Training courses - Group discussions, e.g. on drug policy, medical procedures, drug administration and patient care.</td>
<td>Lectures and seminars - Training courses.</td>
<td>Lectures and seminars - Training courses.</td>
</tr>
</tbody>
</table>

2.14 Drug-related Areas in Need for Training and Education:

The reported areas in need for training (table, 9) present the views of the interviewees. They will give an idea about the training needs at the study hospitals, and do not exclude other areas.

Physicians:

Physicians at the university hospital listed the following drug-related areas:

- Choice of appropriate drugs, dosage forms and route of administration, especially for junior physicians.
- Using intravenous (iv) fluids, particularly for new drugs.
- Therapeutic drug monitoring.
- Drug dosing in hepatic diseases.
- Alternative therapies and new drugs in the market.
- Pain control: dosing of pain killers, timing and duration of therapy.
- Drug-drug and drug-food interactions.
In the private hospital the following areas were reported:

- Use of cardiovascular, respiratory, and renal medication.
- Use of new drugs, chemotherapy and drugs with significant side effects.

As for the MOH hospital, extensive ignorance by many physicians and nurses of drugs and their side effects was pointed out. In addition to:

- ICU and CCU therapy.
- Use of antihypertensive drugs and iv drug administration.

**Pharmacists:**
The following areas were reported for pharmacists’ training and education at the university hospital (table, 9):

- Rationalisation of drug use, its objectives and how to achieve it.
- Antibiotics, anti-diabetics and antihypertensive drugs. A chief pharmacist emphasised the importance of introducing guidelines for the use of these drugs.
- Drug-drug and drug-food interactions.

Whereas the pharmacist at the private hospital reported the following areas for training and education:

- Pharmacokinetics, drug-drug and drug-food interactions.
- Good dispensing practice; vigilant prescription review, generic and branded drug names, and correct spelling of drug names.
- New drugs in market.
- Clinical pharmacy practice, its objectives and applications.

In the MOH hospital, the chief pharmacist generally stated drug use and dosing as the areas in need for training.
Table (9): Drug-related Areas in Need for Training and Education:

<table>
<thead>
<tr>
<th>Pharmacists</th>
<th>MOH</th>
<th>University</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug use and dosing.</td>
<td>1- Rationalising drug use.</td>
<td>1- Pharmacokinetics and drug interactions.</td>
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<td>2- Use of antihypertensives, antibiotics, and anti-diabetic drugs.</td>
<td>2- Good dispensing practice.</td>
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<td>3- Drug-drug and drug-food interactions.</td>
<td>3- New drugs in market.</td>
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<td>4- Clinical pharmacy practice.</td>
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<td>Physicians</td>
<td>1- Drug use e.g. Antihypertensives.</td>
<td>1- Choice of drugs and route of administration.</td>
<td>Use of chemotherapy, CV, renal, respiratory and new drugs.</td>
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<td>2- Critical care therapy.</td>
<td>2- Use of iv drugs.</td>
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<td>3- iv drug administration.</td>
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<td>4- Dosing in hepatic diseases.</td>
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<td>5- Alternative therapies and new drugs in market.</td>
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<td>6- Pain control.</td>
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<td>7- Drug-drug and drug-food interactions.</td>
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<td>Nurses</td>
<td>1- Drug administration, e.g. CV and iv drugs.</td>
<td>1- Chemotherapy, CV and new drugs, and antibiotics.</td>
<td>Chemotherapy, respiratory drugs, antidiabetics, and use of inhalers.</td>
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<td>2- Critical care therapy.</td>
<td>2- iv drug administration.</td>
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Nurses:

In the private hospital, the chief nurse stated the need for education on chemotherapy, antidiabetics, respiratory drugs and use of inhalers (table, 9). In the university hospital, use of chemotherapy, antibiotics, new drugs, digoxin and furosemide was suggested for further training. Staff nurses at the university hospital CCU expressed their need to learn about use of cardiovascular medication. A junior resident at the university hospital believed that nurses needed more training on iv drug administration and continuous infusion. The cardiology consultant at the university hospital pointed out the need for specialised nurses. In the MOH hospital, use of cardiovascular drugs, drugs with severe side effects, as well as use of infusion pumps and iv drug administration were reported.

The interviewees reported other areas for development and training, which were not related to drugs. These included:

1- Patient rehabilitation and counselling services, as well as the psychological aspects of patient care.

2- Home care for patients after discharge.

3- Oral feeds and total parenteral nutrition.

4- Accommodation and catering services at governmental and university hospitals.

It was noticed that the interaction during interviews between the chief and staff nurses at MOH hospital elicited more information. The chief nurse, who was interviewed first, was reserved and did not report any limitations when asked about the factors which impeded nurses’ functioning or drug utilisation. However, this was nullified by the staff nurse, who discussed system limitations amply. This had probed the chief nurse, who subsequent to the staff nurse’s reports became more elaborative, changed some of her previous reports and disclosed information on hospital limitations and unavailability of resources.
2.15 The Experience of Clinical Pharmacy Practice at the Royal Medical Services (Army Sector):

2.15.1 Background:

The idea of introducing clinical pharmacy practice to the army sector was first discussed in 1994. In 1996, a pharmacy residency program commenced, comprising two branches: a clinical and a supply. The supply branch involved training pharmacists in drug procurement, storage and inventory. A year later, this branch ceased and the program became solely a clinical pharmacy residency program. It comprised a four-year residency program, followed by a two-year Masters course in clinical pharmacy. It started with seven pharmacists. At the time of interviews, in 2001, there were no clinical pharmacy graduates, hence, clinical pharmacy practice was not yet started. One exception was in the dialysis and oncology wards, where two clinical pharmacy residents were officially practising. Their duties involved drug procurement, dose calculation and follow up of therapy. The first class graduated in 2002 with three students, who were considered the nucleus of clinical pharmacy practice at the army sector.

2.15.2 Aim of the Clinical Pharmacy Residency Program:

The introduction of clinical pharmacy practice aimed at:

- Developing pharmacy profession and expanding the role of pharmacists.
- Devising a system for pharmacists’ classification, through which promotions and privileges will be determined. This will create incentives for pharmacists. As for those who do not wish to join the program, they will be classified depending on years of service in the army.
- Providing proper pharmaceutical care to patients, minimising drug waste and rationalising costs.

2.15.3 Facilitators and Challenges of the Clinical Pharmacy Residency Program:

Learning about the facilitators and challenges of the introduction of clinical pharmacy practice to the army sector would enlighten the introduction of practice into other sector.
Chapter Two

a) Facilitators:

The success in introducing practice was attributed to the following:

1- Physicians’ support of clinical pharmacy practice.

2- Determination of pharmacy directors at the hospital to expand pharmacy profession and the role of pharmacists.

3- Availability of resources to finance the program and have pharmacists trained abroad.

4- Having motivated pharmacists who believed in the idea and were willing to enroll in educational programs. Pioneer pharmacy residents were described as ambitious, keen on learning, developing their skills and working in patient-oriented settings.

b) Challenges:

On the other hand, several obstacles challenged the inception of the program, these were:

1- Opposition by pharmacists. This was described as one of the toughest challenges. A large number of pharmacists predominantly older generation resisted the program. They were hesitant about changing roles and did not wish to return to studying. The interviewee claimed that opponents felt jealous or threatened by the new generation of clinical pharmacists, because of the wide gap in skills and knowledge between them. Nonetheless, dedication to the program, eventually, led to its success. Change in opponents’ behaviour to support the program was reported, as it became clearer to them and they started realising its benefits.

2- Inadequate number of pharmacists to run the program.

3- High workload on clinical pharmacy residents, as they were carrying out traditional pharmacy roles such as dispensing and inventorying etc., due to the inadequate number of pharmacists to provide these services. It precluded residents from focussing on their clinical pharmacy training.
2.15.4 Pharmacists Input Before and After Clinical Pharmacy Practice and its Impact on Physicians’ Practice:

The pharmacist commented on the new role as a clinical pharmacist that they are becoming more patient rather than product-oriented. The traditional roles mainly involved drug procurement, storage, and inventory. Patient counselling services did not exist before the introduction of the clinical pharmacy residency program. Interaction with patients was described as brief, due to high workload, and limited to outpatients. After the introduction of the program, pharmacists participated in medical rounds, reviewed medication charts, answered medical team’s questions on drugs and monitored therapy. Moreover, the pharmacists reported interacting with inpatients, informing them of drug names, use and side effects. Also, encouraging them to comply to therapy. Positive impact of interaction on patients was noticed by the pharmacist.

Furthermore, the pharmacist noted that their participation in medical rounds made physicians more attentive to medication use. However, as clinical pharmacy practice was not yet officially implemented, it was premature to discuss its impact on medical practice. Nonetheless, the pharmacist reported that there were many indicators on excessive drug use, drug waste and medication errors. At present, the RMS have no drug use review or audit systems. Only regulations to control dispensing existed. Wrong use of drugs by patients was also stated and ascribed to inadequate patient counselling, due to the high workload on physicians, pharmacists and nurses.

Clinical pharmacy services were believed to rationalise and enhance appropriate drug use, and to minimise waste. The pharmacist visualised the process of drug use rationalisation as a triangle, whose poles were the physician, the pharmacist and the patient (figure, 9). In order to successfully rationalise drug use, optimal and integral interaction among these three poles was essential. Hence, the physician should optimise prescribing, the pharmacist should review prescriptions and dispense medication accurately, and the patient should comply to therapy and use drugs correctly.
2.15.5 Continuing Education Activities for Pharmacists at the RMS:
The following continuing education activities were reported:
- Lectures once or twice weekly, and workshops.
- Training pharmacists on interviewing and counselling patients, communication and presentation skills.
- Disease management and pharmacokinetics.
- Preparation of daily reports and case presentations, in addition to attending physicians’ continuing education activities.

2.15.6 Views on the Introduction of Clinical Pharmacy Practice to other Settings:
Advice by both RMS pharmacists on the introduction of clinical pharmacy practice to other settings was limited. Because of their little knowledge on the other hospitals’ circumstances, initiatives within administration, and HCPs’ views on the clinical pharmacy practice. Nonetheless, they predicted its success at the governmental and university hospitals, judging by their similarity to the RMS hospitals. All the three settings are public facilities and share the same objectives of providing proper service, optimising therapy outcome, rationalising resources and minimising costs. Teaching hospitals were assumed to welcome clinical pharmacy practice to fulfil the objective of educating and training professionals.
In contrast, the success of clinical pharmacy practice at private hospitals could not be predicted. The pharmacists elaborated that a considerable share of the private hospitals’ profit depended on selling medication.

Regardless of the type of sector, the pharmacists asserted the importance of support by administrative personnel when introducing clinical pharmacy services. High financing was not believed to be required if qualified pharmacists already existed. Good training of pharmacists was reported as the second step in the introduction of clinical pharmacy services.

At the time of interviews the MOH was sponsoring the education of its pharmacists by sending them to study clinical pharmacy abroad. These pharmacists were expected to establish clinical pharmacy practice at the MOH hospitals. At the university setting, there was no pharmacy practice, but serious plans for its introduction existed at King Abdullah university hospital, which were awaiting the graduation of clinical pharmacy students.

2.15.7 An Update on the Program Progress:
The first class of clinical pharmacists graduated in 2002, it comprised 3 pharmacists. One was allocated at the oncology department, the second at the internal medicine department, while the third was training clinical pharmacy residents. In 2004, the program was reportedly in progress, with numbers of clinical pharmacists increasing. New graduates were expected to start practising in 2005. Yet the program was still described in its infancy stage.
Discussion:

The interviews generated valuable information on the Jordanian health care system, which allowed better understanding of health care, particularly at secondary care level. To the best of the researcher's knowledge, this is the first study to describe the Jordanian health care system through combining literature review and interviews with key health care professional. The themes presented in the interviews provided a greater depth of exploration than what has been published in the literature. The interviews are also the first attempt to describe the hospital system in terms of workflow, role of HCPs, factors which influence medical practice, drug use and patient care.

Drug Procurement Policies and Drug Availability:

The differences between the drug procurement policies in the three hospitals stem from the variation in the abundance of resources between the public and the private sectors. The reported higher availability of resources and drugs in the private hospital in the face of the limited resources in the public hospitals conform to what has been previously published in the literature (JNHA, 2000). However, the interviews provided further exploration of the factors that determine drug availability at hospitals. Similarly, the centralisation of procurement and allocation of drugs at the MOH and the university hospitals, and the resultant drug shortages agree with the literature reports on high centralisation within the public sector, as shown in chapter one (WHO, 2003; Otoom et al, 2002b; World Bank, 1997). The decentralisation of decision-making at hospitals as suggested by the university physician is in harmony with the calls in the literature for granting more autonomy at the institutional level (WHO, 2003; JNHA, 2000).

The irrational and excessive drug prescribing patterns at primary health care facilities in Jordan (Otoom et al, 2002a), seem to also extend to secondary care facilities as reported by the interviewees. However, it was not possible to further comment on the level of irrational prescribing practice due to the absence of quality assurance framework. Furthermore, the consequences of physicians' practice of over-prescribing medication at the university hospital, or issuing extra refill prescriptions to save patients the need to
frequently visit the hospital pharmacy, need to be investigated. In other words, is this practice effective, as claimed, in minimising the interruption of therapy because it provides patients with drug supply for a longer period of time, or does it possibly result in drug overuse by the patients. The latter assumption was made in the light of the reported poor patient counselling on medication. Another implication of this practice is that the issuing of false prescriptions will introduce errors into the patients’ records.

*Medical Team Rounds, Members and Duties:*

It is a real challenge for the physicians at the study hospitals to adequately address and appropriately provide the different aspects of patient care within the reported time of 5-10 minutes per patient. The short physician-patient time further raises questions on the appropriateness of therapy decisions, which is one of many other tasks done during the medical round. This is even more challenging in general wards than in specialities, due to the higher diversity of patient casemix and management procedures. Longer consultation time allows attention to more care issues and correlates positively with patient satisfaction (Dugdale et al, 1999). It is difficult to ask physicians, particularly at the public hospitals, to spend more time with the patients, given the high workload and inadequate staffing. Nonetheless, the physicians should be urged, as much as possible, to interact with patients, involve them in the care process, and address the disease implications on patients’ lives. Establishing eye contact, rapport and a trusting relationship with patients, encouraging them to share their concerns, and understanding their backgrounds and beliefs on diseases were identified as vital measures to enhance adherence to therapy (Pelegrin, 2003; Vieder et al, 2002; Boeyink, 1997; Peck and King, 1982; Gillum and Barsky, 1974). Patient dissatisfaction due to poor interaction with physicians, particularly at the university and the MOH hospitals, correlates with reports from the international settings on patients’ dissatisfaction with short consultation time and lack of conversation with doctors (Gascon et al, 2004). There is no consensus in the literature on the “ideal time” to spend with patients. In one study, the adequate time of consultation was described as *the amount of time necessary to properly address all outstanding issues and questions* (Vieder et al, 2002).
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Communication Among Health Care Professionals:
Effective inter-professional communication is essential for enhancing the quality of patient care, drug use, staff performance, and job satisfaction (Daly, 2004; Schmid and Svarstad, 2002; Trombetta and Rogers, 1988). Poor communication among HCPs is one of the primary reasons for medication errors (Doherty et al, 2004; Benjamin, 2003; Dean et al, 2002). The communication between HCPs (physicians and nurses) and pharmacists in all the study hospitals was poor due to the limited clinical role of pharmacists and the absence of multi-disciplinary care programs. The communication with pharmacists was further inhibited by the physicians’ perceptions of the inadequacy of pharmacists’ knowledge on clinical drug use. The conflicting reports of physicians and pharmacists on their level of communication further reflects dissonance between the two professions. Verification of the pharmacists’ reports on providing drug information to HCPs was not possible due to the absence of documentation of their activities.

Medical Practice and the Choice of Drug Therapy:
The interviews uncovered an array of overlapping and interacting factors which influence the Jordanian medical practice and prescribing habits. The setting-related factors reported to impede patient care at the public hospitals, particularly the MOH hospital, such as the unavailability of drugs and under-staffing further explain what Mawajdeh et al (1997) found on long hospitalisation periods at public hospitals due to factors other than the patients’ medical condition.

The low income level and incentives, and the high workload reported at the MOH and the university hospitals are known factors to decrease job satisfaction (Probst et al, 1997). They explain the shifts in health manpower from the public to the private sector, which is leaving the public sector struggling with inadequate and dissatisfied employees.

The diversity in prescribing practice even when treating similar medical conditions raises questions on the appropriateness of, at least, some of the practice. Diversity is predicted due to the lack of practice standardisation. Unfortunately, no data are available
in the literature on the assessment of the appropriateness of the ongoing practices.

The claims by the university physician that practice at the private sector is influenced by practitioners’ wish to increase their profit corroborate what the literature stated on how the method of reimbursing private HCPs on a fee-per-service basis encourages ordering unnecessary services (JNHA, 2000).

The impact of pharmaceutical promotion on physicians’ knowledge and prescribing habits has been addressed in many settings (Buken and Yegenoglu, 2003; Lal, 2001; Chren and Landefeld, 1994). Physicians’ interaction with the industry has been associated with non-rational prescribing, rapid prescribing of new drugs, and less generic prescribing (Wazana, 2000). In Jordan, the situation is no different from the international setting, as reflected by the prevailing branded prescribing habits, whether at hospitals, as reported in this study, or in primary care facilities (Otoom et al, 2002a).

**Patient Counselling Services, Satisfaction and Compliance:**

The poor patient education at the study hospitals, particularly the public hospitals was substantiated by the many examples on patients’ erroneous use of medication, non-adherence to therapy, and the resultant re-hospitalisation. This highlights the need to address patient compliance, which is still an under-investigated area in Jordan. In fact, the interviewees reported several characteristics of the patients at the study hospitals, which were shown to foster non-compliance. These included poor education and low socioeconomic class (Hudson et al, 2004; Khalil and Elzubier, 1997; Levy et al, 1982). Other factors associated with therapy non-compliance are old age and poor patient education on diseases and drugs (Pelegrin, 2003; Boeyink, 1997; Khalil and Elzubier, 1997). Furthermore, inattention to patient preference yields non-compliance, and consequently failure of the disease management. Eventually, this could result in hospitalisation and increase the costs of care (Pelegrin, 2003; Khalil and Elzubier, 1997). The hospitalisation of 7% up to 64% of heart failure patients as a result of exacerbation of the diseases was found due to non-compliance to therapy and diet (Tsuyuki et al, 2001; Michalsen et al, 1998; Chin et al, 1997; Ghali et al, 1988).
For these reasons, it is important to address and ameliorate the reported patient dissatisfaction when the prescribed drugs are substituted with alternatives, at the public hospitals. This could be achieved by close coordination between the physician, pharmacist and the patient, and assuring the patients on the effectiveness of the alternative medication (Dowell et al, 1996). Other strategies to enhance patient compliance include negotiating and tailoring therapy regimens to the patients’ needs (Boeyink, 1997; Peck and King, 1982; Gillum and Barsky, 1974), assessing the patients’ beliefs and correcting any misconceptions, educating patients and motivating them through reminders, social and family support (Schroeder et al, 2004; Pelegrin, 2003). Also, simplifying therapy regimens by decreasing the number of drugs or the number of daily doses (Schroeder et al, 2004; Khalil and Elzubier, 1997; Gillum and Barsky, 1974).

Although, explaining to patients how medication works was seen important to overcome non-compliance (Pelegrin, 2003), one of the study physicians believed that such information would be overwhelming to patients, particularly illiterate and low-educated ones. The patient educational level, particularly at the study public hospitals, was reported to determine the amount of information requested by the patients on therapy. Attention to patient educational level is crucial when planning patient education and counselling services.

**Therapy Guidelines:**

The absence of guidelines in the study hospitals is parallel to the case at primary health care facilities (Otoom et al, 2002a). The views of the study physicians on the generalisability of guidelines and not meeting the specific needs of the patients are similar to the physicians’ views in international settings (Cranney et al, 2001). Surprisingly, one of the reasons of opposing the introduction of guidelines by the interviewees was the perception that physicians’ knowledge was satisfactory. It would be interesting to validate such perceptions through the evaluation of the appropriateness of current medical practices.
Generic versus Branded Prescribing:
The prevailing branded prescribing in all the study hospitals correlates to the branded prescribing practice at primary health care facilities in Jordan (Otoom et al, 2002a). Both the interviews and Otoom et al (2002a) study confirm the strong impact of pharmaceutical promotion on doctors’ prescribing habits. It is imperative in settings of limited resources like the MOH and university hospitals to encourage generic prescribing, especially that it was proven to be an effective measure to curtail drug costs (Ahluwalia et al, 1996; Dowell et al, 1995).

Role of Hospital Pharmacist:
Several opportunities for expanding the role of pharmacist were revealed in this stage, such as assisting physicians in therapy decisions, assessing drug use, monitoring therapy, and patient counselling. Opportunities for hospital pharmacists in patient care in Jordan will be discussed in more detail in the light of the evaluation of drug use at hospitals, as shown in the second part of the thesis. It is difficult to extrapolate the experience of clinical pharmacy practice at the RMS hospitals to other settings, due to the autonomy of the different health programs. The assessment of the initiatives within each sector to introduce pharmacy practice is needed.

Drug Information Sources, Continuing Education Activities and Needs:
Having medical representatives as the primary source of drug information for HCPs explains the ongoing branded prescribing patterns and heavy impact of pharmaceutical promotion on medical practice. The reliance on medical representatives for drug information was associated with less rational prescribing (Haayer, 1982). This can also be one of the reasons of the reported irrational prescribing patterns at the study hospitals.

The limited drug information sources used by the pharmacists explain their inability to advise physicians on the clinical use of drugs. Pharmacists mainly used a limited range of references and books, which are not considered among the primary sources of up-to-date evidence-based information (Chan et al, 1996; Price and Goldwire, 1994; Slawson
et al, 1994). None of the pharmacists stated referring to professional journals, evidence-based literature, systematic reviews, or clinical trials, which have been repeatedly stated in the literature as primary sources for evidence-based information (NeLMH, 2005; Phillips et al, 1998; Cook et al, 1995; Guyatt et al, 1995). Furthermore, none of the pharmacists mentioned referring to therapy guidelines, which is attributed to the non-guideline-oriented environment. Several factors can explain why pharmacists do not seek primary sources of evidence-based drug information. One of the factors could be embedded in the pharmacy undergraduate education curriculum, which does not orient students to concepts of evidence-based medicine, the search and critical appraisal of evidence. Another primary factor, particularly at the public hospitals, is the lack or limited availability of internet services, which deprives pharmacist the chance to access this source of ample up-to-date drug information. Additionally, the absence of incentives for continuing education and performance development, as well as the high workload, and lack of clinical practice. All of these eliminate the pharmacists’ need to seek sources of information beyond the limited references currently in use. As a result, the pharmacists are kept behind in terms of their knowledge on the clinical use of drugs.

The areas proposed for training reflect the gaps in drug information sources, continuing education and staff training. The physicians’ request for objective drug information to assist therapy decisions re-enforces the need to counteract the biassed promotional information heavily directed at physicians by the pharmaceutical companies. On the other hand, the suggested areas, such as the appropriate use of drugs, dosing in end organ disease, therapy in intensive care settings, iv therapy, TDM, and drug interaction, can serve as the gateway for a more active role of pharmacists in patient care. Furthermore, they can guide the planning of professional training and continuing education programs.

Despite that the HCPs addressed their systems defects and called for reform. However, for a reform to effectively take place, initiative and coordination must exist at the level of policy makers and hospital administrators to bring about change.
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The interviews raised questions on other important issues in health care, which were not directly related to the project objectives. However, they were believed to be important areas for investigation in future work. Examples of these issues are addressed in the following questions:

• What is the extent of drug waste at health care facilities? How to enhance resource utilisation? What solutions are there other than the decentralisation of management?
• What are the strategies to effectively improve practice and patient care?
• What are the strategies to effectively improve practice and patient care?
• What are the strategies to effectively improve practice and patient care?
• What is the rate and types of medication errors at Jordanian hospitals? What are their causes and consequences? How do they vary across the different sectors?
• What is the rate of drug-related admissions? Which groups and drugs are most involved? How to prevent them?
• What is the level of compliance to therapy among patients in Jordanian settings? How does patients' satisfaction with medical care affect their adherence to therapy? What are the measures to enhance compliance, given the social, environmental, educational and psychological characteristics of the Jordanian population?
• What are the strategies to enhance health care professionals-patient communication?
• What are the barriers to communication among health care professionals? How does poor communication impact patient care? How can it be enhanced?
• How to enhance patient counselling services? Who are the patient groups most in need for the service? How satisfied are the patients with the information they receive?

Undertaking research to answer the above questions is imperative to further understand health-related issues in Jordan and effectively plan strategies to enhance patient care. Also to establish evidence on the need for the lacking services, hence, convince administrators and policy makers to invest in implementing these services.

Limitations:
It is realised that the sample size is small and the themes presented do not include all the existing points of view. However, it could be said with certainty that the interviews describe the general situation at Jordanian hospitals. This is based on the fact that the study hospitals are the major hospitals in the country, particularly the MOH hospital,
which is the biggest hospital in Jordan, and its policies and regulations extend to all other MOH hospitals. Furthermore, the similarities of conditions within each health sector, whether public or private, would allow generalisability of some of the themes such as drug procurement and availability, as well as workload and job incentives across the different settings. The level of depth in which the themes were described, and having key health care professionals from different settings as the majority of the interviewees are believed to compensate for the small sample size. The views of professionals at lower positions were also sought to present different points of view and obtain an overall picture of the hospital systems. Another limitation was during the conduct of the interviews, where two interviewees at managerial positions were noticed to be reserved in terms of disclosing their settings' limitations. This validity issue was rigorously approached through constantly probing the interviewees by repeating the question or asking it differently. Also through triangulation and cross-referencing the reports of the different health care professionals. It was noticed that HCPs at non-managerial positions were more elaborative in describing the shortages in their settings and suggesting reform.

Key Points from the Interviews and Implications for the Next Stage:
The salient points from this chapter, which influenced the planning of the project were classified into three main themes:

I. **Drug procurement, availability and use at the three hospitals:**
- Serious drug shortages exist in the MOH and the university hospitals, as a result of the limited resources and high centralisation of drug procurement and allocation policies. In contrast, there are no problems with drug availability at the private hospital due to the availability of resources. How these variations across the different settings affect the drug use patterns is still under-investigated.

- Irrational and excessive drug prescribing were reported at the three hospitals. Yet, there are no data on the evaluation of the ongoing prescribing patterns in
Jordanian hospitals.

- Prescribing practices are diverse due to the absence of guidelines and standardisation of care. Only at the MOH hospital that guidelines for some diseases were stated to exist, but nothing was reported on their implementation. The diversity in practice, even in treating similar conditions, raises the question on how appropriate the different patterns of practice are.

- Branded prescribing habits are prevailing in all the hospitals, due to the heavy impact of pharmaceutical promotion on physicians' practice. Medical representatives are the primary source of drug information for physicians and pharmacists in all hospitals. This has been proven in international settings to be associated with irrational prescribing practice. Again, no data are available in Jordan on the impact of drug promotion on the soundness of drug utilisation.

II. Inpatient care and factors perceived to influence medical practice:

- High workload, low income and incentives, as well as understaffing are limitations reported by the MOH and university HCPs, which were perceived to impede practice and patient care. Conversely, higher income, better incentives, less workload, and adequate staffing were reported at the private hospital. The evaluation of drug use at the different sectors would identify how the variations among the sectors impact current practice.

- In the three hospitals, medical rounds were short (5-10 minutes/patient), involved a big number of patients and a variety of casemix. Many activities are performed during the rounds, which does not leave enough time to adequately address all aspects of care. This raises speculations on the appropriateness of the drug therapy decisions made within all of these constraints.
III. Role of hospital pharmacist:

- In all the study hospitals, pharmacists do not have a role in patient care. Care for inpatients, choice of drugs, therapy monitoring and follow up of patients are exclusively done by the physicians. Clinical pharmacy services either do not exist or are still under-developed. The pharmacists' roles mainly revolve around drug procurement, storage and inventory. Their interaction with patients is limited to the outpatient settings, where they briefly provide instructions on drug use. All pharmacists expressed their wish to have an active role in patient care. However, the opportunities for pharmacists' contribution in patient care still need to be investigated.

- The proposal to introduce clinical pharmacy practice was welcomed by all the interviewees in all the hospitals. The RMS pharmacists were optimistic about their experience in implementing clinical pharmacy services and stated being supported by other HCPs. They predicted the success of clinical pharmacy practice in other public hospitals, but not private ones.

In conclusion, the above findings raised questions on the appropriateness of drug use at Jordanian hospitals, which could not be further explored due to the absence of quality assurance measures and drug use evaluation activities. This rendered drug utilisation a priority area to investigate, and directed the project towards the evaluation of drug use practices. On one hand, it will allow identifying the gaps in practice, and subsequently the areas for improvement. Furthermore, it will explore the opportunities for hospital pharmacists in patient care.

The use of cardiovascular (CV) drug at Jordanian hospitals was chosen as the domain of the project. This is primarily due to the high burden of cardiac diseases in Jordan, which would render the findings of the project more valuable to the local settings. Moreover, CV medication fulfil the criteria for conducting DUE activities, as advised by some professional reports (ASHP, 1996; Kubacke, 1996; Krichbaum et al, 1990), which are also applicable to the Jordanian setting. These include:
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- Expensive medication.
- Received by a large number of patients.
- Used for life-long periods.
- Their suboptimal use would negatively impact patient outcome and system costs.
- They possess high potential for serious side effects and adverse drug reactions if not appropriately used e.g. thrombolytics, anticoagulants, and antiarrhythmics.

In part two of the thesis a hospital-based study to describe and evaluate the use of cardiovascular medication at Jordanian hospitals is presented. Consequently, gaps in practice will be identified, and recommendations to enhance practice and involve pharmacists in patient care will be discussed.
PART TWO
Chapter Three:  
Cardiovascular Diseases Management and the Role of Pharmacist in Cardiac Patient Care.

Introduction:
In chapter one, it has been illustrated how cardiovascular diseases (CVD) are a major health burden in Jordan. They are responsible for 40% of all deaths and are one of the primary causes of hospitalisation (Khoury et al, 1999; Hijazi, 2005). This profile is similar to other developed and developing countries. In USA, 37% of all deaths are attributed to CVD, primarily coronary heart diseases (CHD) and heart failure (HF), which constitute 53% and 6% of CVD deaths, respectively. This makes CHD the single largest killer in America, causing 20% of all deaths (AHA, 2006). Similarly, in UK, CVD cause 38% of all deaths, half of these are due to CHD. Whereas, HF is estimated to exist in 0.9 million adults (BHF, 2005).

CHD and HF are chronic diseases with serious ramifications on patients' lives and well-being. The realisation of how crucial appropriate management of these diseases is, and how drug therapy is a mainstay in determining patients' prognosis. Furthermore, there is a paucity of clinical data on prescribing patterns in cardiac diseases at secondary care level in Jordan. All of these directed the project into investigating the drug utilisation patterns in cardiac diseases at Jordanian hospitals.

The second part of the thesis involves a descriptive study of the prescribing patterns in hospitalised cardiac patients, the development of a tool for the assessment of CV drug use, and eventually the application of this tool to evaluate the ongoing prescribing practices of CV drugs at three Jordanian hospitals. The results would inform on what opportunities are there for pharmaceutical care at Jordanian settings.

This chapter presents an overview of drug therapy in CVD, pharmaceutical care for cardiac patients, and the methods used to assess CV drug utilisation. The chapter is divided into three sections. The first section presents evidence-based management of
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CHD and HF, focusing on the use of CV medication. The second section highlights the opportunities for pharmaceutical care in cardiac patients, and pharmacists' role in optimising and rationalising drug use. Finally, the third section explores the different approaches to drug use evaluation (DUE), the study designs and data collection methods, indicating the advantages and limitations of the different methods.

Section I. Management of Coronary Heart Diseases and Heart Failure.

Pathophysiology:
Coronary heart diseases (CHD), also known as coronary artery diseases (CAD), are mainly caused by narrowing of the coronary arteries due to atherosclerosis (plaque). Consequently, the blood supply to the heart fails to meet its demand for oxygen a condition known as ischemia. In stable angina (SA), ischemic symptoms manifest during exercise as a result of failing to meet the increased heart demand for oxygen. Whereas, acute coronary syndromes; unstable angina (UA) and myocardial infarction (MI), occur due to the occlusion of coronary arteries upon thrombus formation following the disruption of plaque. The occlusion is partial in UA, while it is complete in MI resulting in death of the myocardial tissue due to prolonged ischemia (Grech, 2003; Alpert et al, 2000).

HF is classified into systolic and diastolic dysfunction (Gilmore, 2003). The systolic dysfunction HF, which is the more common type, is characterised by impaired left ventricular function, and reduced cardiac output and ejection fraction. Hence, the heart fails to efficiently pump the blood to meet the body’s metabolic demand. This triggers a sequel of compensatory mechanisms, which are, first, the activation of the sympathetic nervous system to provide inotropic support and maintain cardiac output. However, prolonged sympathetic stimulation leads to worsening of the cardiac function. Second, the activation of the renin-angiotensin-aldosterone system, resulting in vasoconstriction of systemic and renal arteries, and triggering the release of Aldosterone, and sodium and water retention (Jackson et al, 2000). Hence, the patient suffers symptoms such as edema, shortness of breath and reduced tolerance to exercise.
Clinical Management of CHD and HF:
The management of CHD and HF has been amply discussed in the literature. Benefits of CV medication in treating cardiac patients have been clearly illustrated by many studies, as presented below. Large randomised controlled trials (RCT) were mainly sought, during literature review, because they constitute a primary source of evidence-based data.

**Beta-blockers:** These are popularly used drugs with proven effectiveness in the management of CHD and HF. They decrease blood pressure, heart rate and contractility, which improves myocardial perfusion and reduces its oxygen consumption (Borrello et al, 2003; Gibbons et al, 2002). Furthermore, they decrease the number and duration of ischemic episodes in SA patients, as illustrated in the TIBBS trial with bisoprolol (Von Arnim et al, 1995) and the IMAGE trial with metoprolol (Savonitto et al, 1996). In MI, beta-blockers were reported to limit infarct size, relieve pain and reduce the incidence of arrhythmia (Van de Werf, 2003). They significantly reduce mortality, re-infarction and/or sudden death in acute as well as post acute MI patients. This was shown by several RCT such as the ISIS-1 trial with atenolol (1986), the MIAMI trial with metoprolol (1985), the BHAT trial with propranolol (1982), the Norwegian trial with timolol (1981), and the CAPRICORN trial with carvedilol (2001).

In HF patients, beta-blockers were shown to significantly alleviate symptoms, improve quality of life, reduce mortality, frequency and length of hospitalisation (Shibata et al, 2001; Hjalmarson et al, 2000; Packer et al, 1996).

**Angiotensin Converting Enzyme Inhibitors (ACE-Inhibitors) and Angiotensin Receptor Blockers (ARBs):** ACE-Inhibitors significantly reduce death, MI and cardiac arrest in stable angina patients, as presented in the EUROPA trial (2003) with perindopril and the PEACE trial with trandolapril (Braunwald et al, 2004). Their use in acute MI significantly reduces mortality (ISIS-4, 1995; GISSI-3, 1994), as well as their early initiation in post MI patients, whether with left ventricular systolic dysfunction (LVSD) (Pfeffer et al, 1992) or without LVSD (AIRE study, 1993).
ACE-Inhibitors were also established as a primary HF therapy. They significantly lower mortality, morbidity and hospitalisation due to worsening HF (Garg and Yusuf, 1995; Yusuf et al, 1992; CONSENSUS trial, 1987). Nonetheless, some patients develop intolerance to ACE-Inhibitors. In these groups, ARBs can be alternatively used. The CHARM-Alternative trial proved effectiveness of candesartan, an ARB, in significantly lowering mortality and hospitalisation in HF patients intolerant to ACE-Inhibitors (Granger et al, 2003). The same outcome measures were achieved in the CHARM-Added trial, where candesartan was added to ACE-Inhibitors in HF patients (McMurray et al, 2003). Despite this latter study, the analysis of co-existing evidence and the views of HCPs favour the use of ACE-Inhibitors over ARBs unless intolerated (McMurray et al, 2004; Davies et al, 2000).

**Diuretics:** These are established HF therapy. Because they increase urinary sodium excretion, diuretics reduce peripheral edema and alleviate HF symptoms (Cowie and Zaphiriou, 2002; Hunt et al, 2001). Loop diuretics and thiazides improve exercise tolerance (Parker et al, 1993; Haerer et al, 1990), and decrease mortality and hospitalisation due to worsening of HF (Faris et al, 2002). Their appropriate use in combination with beta-blockers, ACE-Inhibitors and digoxin is essential in the successful management of HF (Swedberg et al, 2005; Hunt et al, 2001). On the other hand, spironolactone, a potassium sparing diuretic, was shown to significantly reduce the risk of mortality and hospitalisation in patients with severe HF (Pitt et al, 1999).

**Anti-platelets, Anticoagulants and Thrombolytics:** Evidence has been well established on the importance of aspirin in the prevention and prophylaxis of CHD (Bredie et al, 2003; Juul-Moller et al, 1992). Ridker et al (1991) reported a significant reduction in the risk of MI in SA patients with the administration of aspirin by 87%. The CURE trial demonstrated benefits of clopidogrel in addition to aspirin in UA patients, where it significantly reduced CV mortality, MI and stroke (Peters et al, 2003). Heparin is also recommended in UA patients as it significantly reduce the incidence and duration of ischemic attacks (Neri Serneri et al, 1995). The early administration of aspirin and heparin in acute MI significantly reduced mortality in the ISIS-3 trial (1992) in
comparison to aspirin alone. Similarly, the early initiation of fibrinolytics in acute MI patients substantially reduced mortality as in the GISSI trial on streptokinase (1986). Moreover, the combination of aspirin and streptokinase in acute MI was more beneficial than each drug alone, because of their additive effect (ISIS-2, 1988). On the other hand, the combination of heparin and alteplase (t-PA) was significantly associated with lower rates of death and stroke than with streptokinase and heparin (GUSTO trial, 1993a). This was explained by the accelerated restoration of coronary flow induced by t-PA, resulting in improved myocardium function, hence lower mortality (GUSTO, 1993b).

**Anti-lipids:** The benefits of lowering cholesterol and LDL in the primary and secondary prevention of acute coronary events have been proven by several large trials. The Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) showed how lovastatin significantly prevented UA, fatal and non-fatal MI, and sudden death in patients without clinically evident CVD and with average cholesterol and LDL levels (Downs et al, 1998). Similarly, the WOSCOPS study found pravastatin significantly preventing MI and cardiac death in men with hypercholesterolaemia and no history of MI (Shepherd et al, 1995). The secondary prevention of coronary events in CAD patients was evident with simvastatin in the 4S trial (1994) and pravastatin in the LIPID trial (1998). Both trials indicated lower mortality from CHD, MI, stroke, and coronary revascularization with the lowering of cholesterol levels. Similar benefits were achieved even in CHD patients with average cholesterol levels (Sacks et al, 1996).

**Digitalis:** Digoxin is the most commonly used member of the digitalis family. In HF, digoxin is used to alleviate symptoms and increase exercise tolerance as it improves myocardium contractility (Cowie and Zaphiriou, 2002; Hunt et al, 2001). It was shown to significantly reduce the rate of hospitalisation both overall and due to worsening HF (p <0.001) (Garg et al, 1997). In the same study, despite not reducing the overall mortality in HF patients, digoxin (versus placebo) showed a trend towards lower mortality due to worsening HF (p=0.06).
**Nitrates:** Through inducing vasodilatation and reducing the preload, nitrates reduce the left ventricular volume and arterial pressure, which decreases myocardium oxygen demand and consumption, hence relieve ischemia (Gibbons et al, 2002). They alleviate ischemic pain, decrease the frequency of ischemic attacks and improve exercise tolerance in CHD patients (Braunwald et al, 2002; Schneider, 1988; Hirota et al, 1987). Evidence, however, supports using nitrates in combination with other drugs such as beta-blockers and/or CCB for optimal management of ischemia (Heller et al, 1997). Similarly, nitrates were used in combination with hydralazine in HF. The V-HeFT I trial, demonstrated a 28% reduction in mortality with the nitrate-hydralazine combination over placebo in HF patients (Cohn et al, 1986). However, a subsequent trial, the V-HeFT II, compared the nitrate-hydralazine combination to enalapril, proving the superiority of ACE-Inhibitors in mortality reduction in HF (Cohn et al, 1991). Currently, the nitrate-hydralazine combination is less favoured and suggested as an option in patients with severe renal impairment, who can not tolerate ACE-Inhibitors or ARBs (Cowie and Zaphiriou, 2002; Davies et al, 2000).

**Calcium Channel Blockers (CCB):** CCB were shown to reduce the frequency and duration of ischemic attacks and improve exercise tolerance in SA patients (Heller et al, 1997; Savonitto et al, 1996; Von Arnim et al, 1995). Furthermore, they considerably lower mortality in post MI patients without HF as illustrated in the DAVIT II trial (1990) with verapamil vs placebo. On the other hand, Hansen et al (1997) compared the combination of ACE-Inhibitors and diuretics with and without CCB in HF patients post MI. The study illustrated significant reduction in MI, UA and hospitalisation due to HF in the CCB group.

**Conclusion:**
In summary, CHD and HF are chronic diseases with serious implications on patient mortality, morbidity and quality of life. The effective management of these diseases is crucial and have important economic implications, as it would considerably reduce the burden of these diseases. Having reviewed the literature, evidence has been clearly established on the benefits of CV drugs in alleviating the symptoms and improving the
Chapter Three

prognosis of CHD and HF patients. Nevertheless, the appropriate use of these drugs is essential for achieving the aimed therapy goals. It is one of the pharmacists' primary roles to assure the appropriate use of medication. The following section presents the opportunities and responsibilities for pharmacists in cardiac patients care.
Section II. Pharmaceutical Care for Cardiac Patients: Pharmacists’ Opportunities and Responsibilities.

Introduction:
The benefits from involving pharmacists in patient care have been demonstrated, which grants pharmacists more opportunities for a greater role in patient care than in the past. The management of cardiac diseases is multi-faceted, and a multi-disciplinary approach to it has been encouraged (Lock, 2003; Coombes et al, 2002). It is a complex and long process due to the chronic nature of cardiac diseases, which comprises risk factor modification, drug therapy optimisation, patient monitoring and follow up, patient counselling and support to enhance their adherence to medication.

In Jordan, the continuously increasing cardiac patient demand, the high pharmaceutical spending, the irrational drug use and the poor patient counselling on medication, as reported in chapters one and two, uncover the variety of opportunities for pharmacists’ contribution in patient care. The following are examples of the pharmaceutical care services which pharmacists can provide to optimise cardiac patient care, substantiated by evidence from the international literature. Table (10) shown at the end of this section provides a summary of key studies, which illustrate the effect size of pharmacists’ interventions on patient outcome and professional activity.

Pharmaceutical Care on Admission:
Admission pharmacists, distinctive from ward pharmacists, have an important role of confirming accurate medical and drug history (Brady and Dean-Franklin, 2004; Brady, 2003; Robb et al, 2003; Gurich, 1983). Pharmacists were found to obtain a more thorough drug history than physicians (Gurich, 1983). This could be attributed to the pharmacists’ wider knowledge of the different drug formulations, physical shapes and OTC medication. The identification of drug history allows the accurate transfer of information from primary to secondary care level. Hence, it ensures continuity of therapy and minimises the possibility of prescribing incompatible drugs to the drug history. Moreover, it allows early recognition of any drug-related problems (Brady and
Chapter Three

Dean-Franklin, 2004; Robb et al, 2003; Brady, 2003; Thornton, 1996). Admission pharmacists also assess patient’s own drugs for suitability to use on ward or on discharge (Booth, 2000). The participation of these pharmacists in post-admission rounds was advocated to further assure safe prescribing (Brady and Dean-Franklin, 2004).

**Reviewing Prescriptions and Optimising Drug Use During Hospitalisation:**

Rigorous review of prescriptions and the assessment of therapy to assure appropriate drug prescribing is one of the primary responsibilities of pharmacists. Considerable reduction in mortality, morbidity and re-hospitalisation of HF patients have been achieved with the interventions of a clinical pharmacist to optimise ACE-Inhibitors use and adjust therapy to patient-specific needs (Luzier et al, 2000; Gattis et al, 1999). The cost savings achieved from such intervention were substantial, indicating cost-effectiveness of clinical pharmacy services (Luzier et al, 2000; Rainville, 1999). Moreover, pharmacists can intervene effectively to identify, prevent and resolve medication errors and drug adverse events (Robb et al, 2003; LaPointe and Jollis, 2003; Booth, 2000; Gattis, 1999; Chisholm et al, 1995). They were reported to participate in preparing, delivering and administering parenteral drugs, such as antiarrhythmic drugs (Robb et al, 2003) and thrombolytics (Krichbaum et al, 1990). They can also assist speciality teams in addressing pharmaceutical issues outside their speciality area (Larsson and Cavey, 2003). They have a crucial role in care for critical patients, such as myocardial infarction patients or those undergoing cardiac surgery. Pharmacists were reported to advise on intravenous drug dosing, compatibilities and calculations of flow rates (Robb et al, 2003). In post-surgery care, they ensured adequate analgesia, prophylactic antibiotic therapy and cardiac function support (Booth, 2000).

**Therapy Monitoring and Follow Up of Patients:**

This is another key area in cardiac patient care to which pharmacists can effectively contribute. Monitoring therapy is essential to assess patient response to treatment, identify any problems, and adjust drug regimens accordingly. For instance, monitoring therapy in angina patients to assure relief of ischemic pain, or diuretic therapy in heart
failure patients to alleviate edema. Better reporting of adverse drug events was found in response to pharmacist-led monitoring and reporting programs (Wee and Low, 2001). Pharmacists with their unique expertise in pharmacokinetics and pharmacodynamics can advise on drug dosing and maintenance regimens, in cases where drug excretion can not be measured, as in renal and hepatic failure (Thomson, 2003). Monitoring of digoxin was found to significantly improve when supervised by pharmacists, who advised on the correct drug sampling times (Vitillo, 2001). This would minimise the risk of digoxin toxicity and enhance patient care (Thornton, 1996).

**Drug Information and Academic Detailing by Pharmacists:**
Pharmacists can serve as a primary drug information source to patients and other HCPs. In the literature, there are many examples of drug educational sessions successfully run by pharmacists to HCPs, such as thrombolytics (Krichbaum et al, 1990), CV medication (LaPointe and Jollis, 2003), beta-blockers (Behan, 2001), CCU medication (Thornton, 1996; Behan, 2001), and digoxin monitoring (Vitillo, 2001). On the other hand, a positive impact of inpatient counselling on medication by a pharmacist has been reported to improve patient knowledge and education on medication (Al-Rashed et al, 2002).

**Pharmacists Role on Discharge:**
In order to enhance seamless transfer of care from secondary to primary level, pharmacists have to ensure clear and efficient communication of drug information to patients before discharge. This would improve drug use and quality of life of patients, and minimise re-hospitalisation. Monitoring of discharge prescriptions by pharmacists resulted in safer prescribing. Pharmacists advised on discharge medication, ensured adequacy of therapy, prevented prescribing errors and provided written instructions on drugs to patients (Dunlap et al, 2003; Elfallah and Jappy, 1996). Moreover, pharmacists can participate in arranging home care and liaise with community health care providers or the patients’ carers on medication (Lock, 2003). Post discharge care by pharmacist can involve contacting patients to answer their queries on drugs, detect problems with therapy, encourage patient self-management and advise on secondary prevention.
measures (Coombes et al, 2002; Al-Rashed et al, 2002; Booth, 2000; Rainville, 1999; Gattis et al, 1999; Thornton, 1996).

**Patient Education and Counselling:**
Pharmacists are ideal candidates to educate patients on drug use, diseases, and life-style modification (e.g. diet and smoking cessation in cardiac patients). They can also encourage patients’ self-management (e.g. record daily weights in HF), undertaking testing (e.g. cholesterol screening and warfarin monitoring), and adherence to therapy (Brady, 2003; Larsson and Cavey, 2003; Talbert et al, 2002; Anonymous, 2001; Tadros et al, 2000; Gattis et al, 1999; Thornton, 1996). Pharmacists should identify reasons for patients’ non-compliance to therapy and find solutions to overcome them (Brady, 2003). Verma et al (1997) illustrated that educating HF patients led to significant improvement in their physical and social functioning, hence their quality of life.

**Quality Assurance and Development of Treatment Protocols:**
Pharmacists can effectively contribute to quality assurance through conducting drug use review and audits, then provide feedback to HCPs on areas in need for improvement (Anonymous, 2001; Thornton, 1996; Krichbaum et al, 1990). They can also engage in developing treatment protocols, drug use evaluation criteria, and clinical pathways to optimise CV drug use (Adcock, 2003; Lock, 2003; Gandhi et al, 2001; Booth, 2000; Lunn et al, 1997; Thornton, 1996; Krichbaum et al, 1990). However, strategies to support the dissemination and implementation of guidelines should be adopted. Axtell et al (2001) illustrated how pharmacists successfully increased the adherence to guidelines.

**Cost Containment and Rationalising Drug Use:**
The situation in most health care systems of limited resources, escalating expenditure and patient demand rendered attention towards cost containment and drug use rationalisation increase. Pharmacists have to liaise with medical staff to ensure that cost-effective drugs are used (Thornton, 1996). Gandhi et al (2001), evaluated the impact of clinical pharmacy services on direct drug costs in CCU. The pharmacist intervened to rationalise drug use, provided staff education, developed and implemented critical
pathways for CV drug utilisation. Significant reductions in drug costs, estimated at $372,384 were reported.

Conclusion:
Many studies have demonstrated the positive impact of pharmacists’ contribution to patient care, and in the context herein, to cardiac patient care. Pharmacists play an important role to assure appropriate and safe use of medication, promote cost-effective practices, and enhance patient care and adherence to therapy. Linking this evidence to the current limited practice of pharmacists in Jordan reveals the versatile opportunities to expand their role in patient care. This will be discussed in later chapters.
Table (10): A Summary of Pharmacist-intervention Studies to Illustrate the Effect Size of Pharmacy Services on Clinical Outcome, Patient Care and Professional Activity:

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>Study Design</th>
<th>Cohort</th>
<th>Study Setting</th>
<th>Medical Condition</th>
<th>Pharmacist-Intervention</th>
<th>Duration/Follow-up</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Schnipper et al (2006)</td>
<td>RCT to determine the effect of pharmacist-led patient counseling on adverse drug events.</td>
<td>178 patients</td>
<td>At hospital discharge and home</td>
<td>General medicine</td>
<td>Counsel patients at discharge, follow up of patients by telephone post-discharge, clarify regimens; reviewing indications, use and side effects, encourage adherence.</td>
<td>51 weeks</td>
<td>Significant reduction in the rate of preventable ADEs in the intervention group (p = 0.01)</td>
</tr>
<tr>
<td>Sadik et al (2005)</td>
<td>RCT</td>
<td>208 patients</td>
<td>Hospital</td>
<td>HF</td>
<td>Counsel and educate patients on disease, medication, and lifestyle modification, instruct patients on self-monitoring, discuss therapy with physicians to rationalise and simplify drug regimens.</td>
<td>12 months</td>
<td>Significant improvement (p &lt;0.05) in heart failure symptoms, exercise tolerance, health-related quality of life, adherence to prescribed drugs and lifestyle advice. Furthermore, less hospital admissions in the intervention group (22 vs 36 admissions).</td>
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</table>
Table (10): Continued.

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<th>Duration/Follow-up</th>
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<tr>
<td>LaPointe and Jollis (2003)</td>
<td>Descriptive and evaluative study of pharmacists’ interventions</td>
<td>14983 pharmacist intervention, of which 4768 to prevent medication errors</td>
<td>Hospital (cardiology wards)</td>
<td>CVD</td>
<td>Participate in medical rounds, review patient therapy, make recommendations to optimise therapy, prevent medication errors, counsel patients at discharge, liaise with physicians and nurses regarding therapy, teach medical staff and nurses.</td>
<td>54 months</td>
<td>Pharmacist interventions led to identifying and preventing 4768 medication errors during the study period.</td>
</tr>
<tr>
<td>Kucukarslan et al (2003)</td>
<td>Single-blind controlled study to evaluate the impact of pharmacist participation in medical round on preventable ADEs</td>
<td>165 patients</td>
<td>Hospital (general medicine units)</td>
<td>General</td>
<td>Participate in medical rounds, evaluate patient records and make recommendations on therapy, clarify drug orders, provide drug information, identify drug interactions, allergy, and system errors.</td>
<td>11 weeks</td>
<td>The rate of preventable ADEs was significantly reduced by 78% in the intervention group in comparison to the control group.</td>
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<td>Al-Rashed et al (2002)</td>
<td>Controlled trial (patients randomized by ward)</td>
<td>83 elderly patients prescribed ≥ 4 drugs.</td>
<td>Before hospital discharge and home</td>
<td>General</td>
<td>Inpatient counseling on drugs and compliance before discharge, home visits to assess drug knowledge, compliance, check home drug stock and health related events.</td>
<td>3 months</td>
<td>Significantly better drug knowledge and compliance in the intervention group (p &lt;0.001). Significantly less outpatient visits and readmission to hospital compared to the control group (p &lt;0.05).</td>
</tr>
<tr>
<td>Zermansky et al (2001)</td>
<td>RCT</td>
<td>1118 elderly patients with ≥1 repeat prescription</td>
<td>General medicine practices.</td>
<td>General</td>
<td>Review drug therapy and make recommendations to physicians.</td>
<td>12 months</td>
<td>Significantly more drug changes (p=0.02), fewer repeat prescriptions (p=0.01), and cost savings (p &lt; 0.001) in the intervention group.</td>
</tr>
<tr>
<td>Gandhi et al (2001)</td>
<td>Evaluation of impact of clinical pharmacy services on drug costs (observational, non-randomized trial)</td>
<td>2879 patients (intervention and control). A total of 4151 pharmacist-led intervention over a 12-month period</td>
<td>Coronary care unit</td>
<td>CVD</td>
<td>Pharmaceutical care services e.g. modify drug regimen to optimize therapy, provide drug information to staff, develop critical pathways for use of CV drugs.</td>
<td>27 months</td>
<td>Significant reduction in hospitalization costs (p&lt; 0.05), and drug costs (p=0.001), with a reduction in total drug costs of $372,384.</td>
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### Table (10): Continued.

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<td>Leape et al (1999)</td>
<td>1- Comparative study; before and after intervention 2- RCT to assess impact of pharmacist (control vs intervention)</td>
<td>275 patients</td>
<td>Medical ICU and CCU</td>
<td>General</td>
<td>Participate in ICU team medical rounds, review medical records, make therapy consultations and assist nurses.</td>
<td>61 weeks</td>
<td>Significant reduction in preventable adverse drug events (by 66%) after the intervention ($p &lt; 0.001$), and by 72% in the intervention vs control group ($p &lt; 0.001$).</td>
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<td>Gattis et al (1999)</td>
<td>RCT</td>
<td>181 patients</td>
<td>Outpatient clinic</td>
<td>HF</td>
<td>Evaluate drug regimens and make recommendations to physicians, educate patients on medication, encourage compliance, and follow up on patients.</td>
<td>6 months</td>
<td>The intervention group has significantly more patients closer to target ACE-Inhibitor dose ($p &lt; 0.01$), more patients receiving alternative therapy if ACE-I not prescribed (75% vs 26%, $p=0.02$), less heart failure events (4 vs 16 death, ER visits, or hospitalization, $p= 0.005$).</td>
</tr>
<tr>
<td>Begley et al (1997)</td>
<td>RCT</td>
<td>190 elderly patients</td>
<td>Home</td>
<td>General</td>
<td>Visit patients at home to provide counseling on compliance and management of drugs.</td>
<td>12 months</td>
<td>Significantly better compliance in the intervention group and fewer outpatient visits ($p &lt; 0.05$).</td>
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<tr>
<td>Boyko et al (1997)</td>
<td>Evaluation of the impact of pharmacists’ intervention on economic and morbidity outcomes (RCT)</td>
<td>867 patients</td>
<td>Hospital</td>
<td>Internal medicine</td>
<td>Participate in medical rounds, review patient charts, and make therapeutic recommendations.</td>
<td>9 months</td>
<td>Significantly shorter hospitalization period (by a mean of 1.3 days), lower pharmacy costs (by $301) and total hospital costs (by $1654).</td>
</tr>
<tr>
<td>Hanlon et al (1996)</td>
<td>RCT</td>
<td>208 elderly patients taking ≥ 5 drugs.</td>
<td>Outpatient clinic</td>
<td>General</td>
<td>Evaluate drug therapy and make recommendations to patients and physicians.</td>
<td>12 months</td>
<td>Significantly lower inappropriate prescribing in the intervention group (p &lt; 0.01).</td>
</tr>
<tr>
<td>Goodyer et al (1995)</td>
<td>RCT</td>
<td>100 elderly patients</td>
<td>Home</td>
<td>HF</td>
<td>Provide intensive drug counseling to enhance adherence.</td>
<td>3 months</td>
<td>Significantly higher compliance, drug knowledge (p &lt; 0.001), higher exercise tolerance (p &lt;0.05), and less peripheral edema (p &lt;0.01) in the intervention group.</td>
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<td>Lipton et al (1992)</td>
<td>RCT</td>
<td>736 elderly patients taking ≥ 3 drugs</td>
<td>At hospital discharge and home</td>
<td>General</td>
<td>Review drug charts and therapy regimens, identify drug-related problems, make recommendations to physician, patient counseling at and post discharge.</td>
<td>3 months</td>
<td>The intervention group had significantly more appropriate therapy regimens (p=0.01), fewer drugs/patient (p &lt; 0.05), less complex regimens (p &lt;0.05), and higher compliance to drugs (p&lt; 0.05) than the control group.</td>
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<tr>
<td>Sidel et al (1990)</td>
<td>RCT</td>
<td>284 elderly patients</td>
<td>Home</td>
<td>General</td>
<td>Provide patient-specific information about drugs, encourage adherence to drugs, stress on good communication with health care provider, home visits and telephone follow up as needed.</td>
<td>11 months</td>
<td>Significantly fewer outpatient visits in the intervention group (p &lt; 0.05)</td>
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Section III: Approaches to the Evaluation of Cardiovascular Drug Use and Prescribing Patterns.

Introduction:
From the previous two sections it becomes clear how crucial the appropriate use of CV drugs is to successfully achieve the required therapy goals. The assessment of drug use is imperative to assure quality of practice and identify areas for improvement. Drug use evaluation (DUE) has been shown to reduce inappropriate prescribing and drug costs. In the light of the reports from Jordan on irrational drug use, high drug expenditure and lack of treatment protocols, it seemed valuable to investigate the ongoing drug use processes at Jordanian hospitals. Unfortunately, there are no data published on this area yet. The literature search generated only two studies, by Otoom et al (2002a and 2002b) and Albsoul-Younes et al (2004), which evaluated drug use in primary care facilities, but not in hospitals.

On the other hand, the international literature has extensively discussed the evaluation of drug utilisation and prescribing patterns. Health services research related to drug use, drug audit, quality assurance and drug use review are all well recognised activities to evaluate and/or monitor the quality of drug use to assure its appropriateness, effectiveness, and/or cost-effectiveness.

This section will present the methods and approaches to DUE, endorsed by examples from the literature, with focus on the use of CV medication. It will also discuss the different study designs and data collection techniques applied in DUE, highlighting the characteristics and limitations of each method. In the light of all the presented methods, the section will conclude with a discussion of the methods chosen in this project to assess CV drug utilisation at Jordanian hospitals.
A) Approaches to the Evaluation of CV Drug Utilisation and Prescribing Patterns:

There are many examples in the literature on the evaluation of CV drug utilisation. Several methods have been used, which are summarised in table (11). Comparing actual practice to pre-defined standards is one of the most common approaches used to evaluate drug use in the CVD area. Under this approach, the methods of developing DUE standards such as the use of guidelines or consensus of experts (table, 11) are discussed, as illustrated below. Additionally, there are several study designs and data collection methods implemented in the DUE studies (table, 11). Examples of the study designs include descriptive and comparative studies, which could be prospective or retrospective, cross-sectional or longitudinal. Data collection methods are mainly the review of medical records, interviews, questionnaires and observation.

Table (11): Methods and Approaches to Drug Use Evaluation:

<table>
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<tr>
<th>Approaches</th>
<th>Study Designs</th>
<th>Data Collection Methods</th>
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<tr>
<td>Methods of developing standards: 1- Extract from evidence-based literature. 2- Use established guidelines. 3- Consensus of experts: - Delphi technique - Consensus development panels - Nominal group “expert panel technique”. - Rand method - Iterated consensus rating procedures.</td>
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<td>II. Peer review of practice.</td>
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<td>III. Medication appropriateness index.</td>
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</table>
Before discussing each of the above mentioned methods, the method of searching the literature to locate relevant studies on the evaluation of CV drug use are presented.

Methods of Literature Search:

The literature search comprised the following resources:

I. Databases and online journals:

   The Searching terms (used in different combinations) were: evaluation, assessment, quality, describe, prescribing, audit, drug audit, clinical audit, guidelines, drug use review, drug utilisation, drug use assessment/evaluation, heart, cardiac diseases, heart diseases, angina, myocardial infarction, treatment, heart failure, beta-blockers, ACE-inhibitors, nitrates, anticoagulants, medication appropriateness index, Delphi, Rand, consensus, cross-sectional.
   - European Journal of Clinical Pharmacology: 1996- 2002. This journal was searched because it was cited several times for information on defined daily doses (DDD); a method used in DUE studies.

II. Bibliographies of the reviewed articles.

III. Hand search of the journals, which were frequently cited in the bibliographies of DUE studies:
   - Pharmacy World Science 2001-02.
   - Prescriber 2001-02. (Recommended by supervisor).

IV. Text books on research methodology.

All searches were limited to the English language.
*Strategy for Searching the Literature on DUE in Jordan:
The literature search was limited to the English language. They involved the following resources:

Searching terms: Jordan, Jordanian hospitals, drug use, drugs, drug utilisation, cardiac diseases, heart diseases (myocardial infarction, heart failure, arrhythmia, congenital heart diseases, or endocardial heart diseases, heart aneurysm, heart injury, heart tumor, or intra-cardiac thrombosis, or ischemic heart diseases, or myocardial diseases, or hypertension, or valvular heart diseases), treatment, cardiovascular agent, cardiac patients, “health care facilities and services”, health care personnel, health care management, health economics, health care organisation, health care quality, disease management, patient care.

2- Hand search of some key journals known for publishing on international health affairs, especially in developing countries. These were:
- Social Science and Medicine, (1995-2006).

3- Several governmental, non-governmental, and academic bodies were contacted to obtain studies and literature on Jordan. These were the MOH, the Department of Communicable and Non-communicable Diseases, the Department of Research and Studies, the MOH information centre, the University of Jordan, the WHO office in Amman and the National Centre for Diabetes, Endocrine and Genetic Diseases.

I. Drug Use Evaluation (DUE) through Comparing Actual Practice to Pre-defined Drug-use Standards:

The importance of performing DUE in a systematic criteria-based process has been emphasised (Bowling, 2002; Kubacke, 1996; Todd et al, 1987). DUE standards should be based on a sound scientific evidence (ASHP, 1996). Drug audit and quality assessment are examples of drug use evaluation against pre-defined standards to assure quality of practice (Bowling, 2002). The most common methods for developing DUE standards are the revision and extraction from evidence-based literature, the referral to already established guidelines and the consensus of experts.
Methods of Developing DUE Standards:

1. Revision and Extraction from Evidence-based Literature:
The literature has been used as a source for DUE criteria in many studies. McMullan and Silke (2001) developed criteria for optimal ACE-Inhibitors dosing in CHF patients based on review of evidence-based literature. Similarly, McAlister et al (1999a) and Mayet et al (1997) reviewed the literature to establish criteria for best care in MI patients and optimal use of anticoagulants in arrhythmia, respectively. In all the studies actual practice was assessed against the developed evidence-based criteria. Consequently, gaps in practice were identified and interventions to improve practice were discussed. However, one main limitation of this method, which should be taken into consideration when reviewing the literature, is that unsystematic reviews would result in unreliable and invalid criteria. Furthermore, there are several areas in practice for which the literature does not provide conclusive answers on best practice, due to inadequate or conflicting evidence, such as the management of arrhythmia.

2. Referral to Established Guidelines:
Established guidelines are a major source of DUE criteria. Examples are guidelines established by major professional bodies such as the British Medical Association, the American Heart Association, the European Heart foundation, the American Society for Hospital Pharmacy, the Scottish Intercollegiate Guidelines Network, the Royal Pharmaceutical Society of Great Britain, and the Agency for Health Care Policy and Research. The use of guidelines, given that they are evidence-based and rigorously developed by professional organisations, eliminates the disadvantage of unsystematic literature reviews. Furthermore, guidelines could involve experts’ opinions to provide recommendations on areas where there is no established evidence, best practice from a pragmatic perspective, or assessment and ranking of available evidence as in the American College such as the guidelines by the American College of Cardiology/American Heart Association for management of ischemic heart diseases. However, the limitations of guidelines as a source of DUE criteria are that they are general and do not fulfil the specificity of patients’ conditions. Also, they are not as up-
to-date as the clinical literature, i.e. they do not usually include evidence from the most recent clinical trials. In all cases, it is crucial to adapt guideline-based DUE criteria to the local setting where DUE is undertaken to assure applicability and suitability of criteria, hence, the validity of the results.

Among the guidelines commonly used in DUE is the British National Formulary (BNF). Wu et al (1998) used the BNF to assess the dosing of antidiabetic, antihypertensive and lipid-lowering drugs. Similarly, Lindley et al (1992) used the BNF to determine the extent of ADRs on admissions related to inappropriate prescribing.

Local guidelines and hospital formularies have been also used to evaluate drug utilisation. Floret et al (2001) assessed the appropriateness of vancomycin use against guidelines published by the hospital infection control advisory committee. Vancomycin use was expressed in the number of courses per 100 admitted-patients and defined daily doses (DDD) per 100 patient-days. Unfortunately, as explained in previous chapters, there are no guidelines or treatment protocols available at Jordanian hospitals, to be used for the assessment of drug utilisation processes.

The defined daily dose (DDD) is a dose standard unit widely used in DUE studies to describe drug utilisation. The DDD is defined as the average dose per day of a drug used for its main indication in adults (Merlo et al, 1996; Dukes, 1993; Serradell et al, 1987; Hekster et al, 1982). The DDD is based on recommendations in the literature, manufacturer’s advice in drug data sheet and experience gained with the product concerned (Dukes, 1993). It was developed to overcome shortcomings of unit cost, packages or prescription volume in expressing drug consumption. As it enables comparison of drug sales and prescription data over time and between regions (Merlo et al, 1996; Dukes, 1993). The applications of DDD included:

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- Examining changes in drug consumption and prescription patterns over time.
- Making international comparisons of drug consumption patterns.
- Evaluating the impact of educational programs on prescribers and patients (Serradell et al, 1987).

On the other hand, using DDD has several limitations, such as:
- It is based on units issued or sold, yet not all drugs reaching the patient are necessarily consumed.
- It is based on standard doses for the major drug indication, and does not necessarily reflect the actual doses prescribed or ingested (Dukes, 1993; Serradell et al, 1987).

One more primary limitation of this method, besides those mentioned above, is that it provides information on the overall consumption of drugs rather than on individual drug regimens (Hekster et al, 1982). In other words, the drug use usually expressed as the number of DDD per 100 bed-days indicates the percentage of patients receiving DDD per day, without identifying the drug regimens in individual patients (Dukes, 1993; Hekster et al, 1982). For this reason, the DDD method is not suitable to use in studies evaluating the appropriateness of actually prescribed regimens or those describing the prescribing patterns in more detail, in individual patients.

3. Consensus of Experts:

The DUE criteria could be either based on already existing consensus statements, as in Walker and McDonald study (2001), where the appropriateness of prescribing proton pump inhibitors was assessed through comparing ongoing practice to existing local consensus criteria. Alternatively, consensus criteria could be developed especially for the purpose of study. In Lunn et al study (1997), criteria for inappropriate prescribing of the most commonly used drugs in a nursing home were developed by one of the study investigators. Later, the criteria were discussed and agreed by an expert panel, then implemented to assess the appropriateness of prescribing practice. Unfortunately, the sources used to derive the criteria were not specified, neither was the method of...
developing them. The study had other limitations, which were believed to underestimate the level of inappropriate prescribing. First, the criteria were developed for the most commonly used medicines only, and in areas where it was easy to agree on them. Thus, the assessment of inappropriate prescribing was limited to those areas only, and it ignored less used medication. Second, criteria were based on prescriptions without considering patients' conditions, hence, whether drugs were indicated for patients or not was not assessed (Lunn et al, 1997). Moreover, basing the evaluation of prescribing practices on criteria for inappropriate rather than appropriate use of drugs would result in further underestimation of inappropriate practices, i.e. if the criteria were incomprehensive and did not include all wrong practices. Conversely, criteria for appropriate drug use would uncover a wider range of inappropriate practices, because any deviation will be considered sub-optimal.

There are three main methods for developing consensus, as illustrated in table (11). Namely, these are: the Delphi technique, the consensus development panels and the nominal group processes 'expert panel'. They are often used in combination and involve a mixture of quantitative and qualitative techniques (Fink et al, 1984). A description of each of these methods, their limitations, validity and the factors that should be taken into consideration when establishing consensus are presented below.

3.1 Methods of Developing Consensus:

3.1.1 The Delphi Technique: This method is based on postal questionnaire, where open-ended questions are used to obtain ideas of participants (experts) individually and anonymously. Responses are compiled into a questionnaire then recycled back to experts, asking them to rank their level of agreement with the questionnaire statements using a numerical scale (Bowling, 2002; Jones and Hunter, 1995; Fink et al, 1984). Commonly, participants are asked to rate confidence or certainty in which they express their opinions (Jones and Hunter, 1995). Rankings of experts are again summarised into a questionnaire and fed back to participants for re-ranking. The re-ranking is analysed, the degree of consensus is assessed and the results are reported to the experts. The
process resumes until consensus is established or returns diminish (Bowling, 2002; Jones and Hunter, 1995; Fink et al, 1984). Beers et al (1991), applied the Delphi technique to develop explicit criteria to assess appropriateness of drug use in elderly patient. The criteria were used in a later study to evaluate drug use in nursing homes (Beers et al, 1992). The Delphi technique has the advantages of preserving the individuals’ identities, being economical and relatively easy, having no geographical constraints on sampling, allowing contact of a large number of people, being applicable to a wide range of topics, and flexible in terms of the number of rounds, which it can be adjusted to the investigator’s needs (Bowling, 2002; Jones and Hunter, 1995; Fink et al, 1984). On the other hand, limitations of this method are that its reliability increases with the size of group and number of rounds. However, panellists usually get tired after 2 or 3 rounds. Besides, the coordination of large groups and several rounds can be complicated and costly. Moreover, the method is subject to the bias of selecting participants. It is crucial that the panel members chosen are experts in the area investigated. Also, this technique is inappropriate if personal contact between participants is required, and is oblivious to reliability measurements and validation of data (Fink et al, 1984). Further concerns on the validity of this technique could be raised with poor design of the questionnaires (Jones and Hunter, 1995).

3.1.2 Consensus Development Panels: this method involves meeting of panels of participants with the aim of developing consensus. A facilitator is required who could be an expert in the field or a non-expert who is credible to participants. This method requires high level of organisation and can be expensive (Bowling, 2002).

3.1.3 Nominal Group Process or the “Expert Panel Technique”: This is a highly structured meeting, where participants (8-12 experts) are asked to individually list their views on the topic in question. Then the panel discusses all the generated ideas, and each participant is asked to privately rank the issues discussed. Rankings are assessed and results are reported to the panel (Jones and Hunter, 1995; Fink et al, 1984). Subsequently, re-ranking takes place in light of discussion (Bowling, 2002; Jones and Hunter, 1995). The success of this method requires a highly trained leader and
cooperation of the panel to work in a structured setting (Fink et al, 1984). One of the applications of this method was to establish priorities for clinical and health services research in critical care in UK and the republic of Ireland (Vella et al, 2000).

3.1.4 The Rand Method: This is a systematic method that combines the Delphi and the expert panel techniques. It has been described as the only systematic method combining expert opinion and evidence (Campbell et al, 2003). It involves reviewing the literature for evidence in relation to the intervention in question. Consequently, generating indications for the intervention, and sending them along with the review to each of the expert panel members. Experts are asked to rank each indication on a nine-point Likert scale (1= extremely inappropriate, 9= extremely appropriate). Later the panel meets and members are reminded of their own ratings and given an anonymous feedback of other panellists’ ratings, then areas of disagreement are discussed. Then re-rating of indications takes place in light of the panel discussion. Finally, the level of agreement is assessed and consensus areas are identified (Bowling, 2002; Hunter et al, 1994). Brook et al (1986) used this method to rate the appropriateness of six medical and surgical procedures, including coronary artery angiography and bypass grafting. A list of criteria for each procedure was compiled based on reviews of the medical literature. Panellists were sent the criteria and the reviews along with rating sheets and instructions on how to use them to rate the appropriateness of each criteria. Levels of agreement and disagreement were analysed. Later, the panel met and discussed the criteria, and had their initial ratings presented along with distributions of the ratings. The panel was asked to re-rank the criteria, levels of agreement were analysed and consensus was established (Brook et al, 1986).

The Rand method has several drawbacks: First, the literature review to develop criteria, if unsystematic, can produce unreliable conclusions. Hence, it is very important to assure that reviews are systematic and well documented (Hicks, 1994). Second, the method ignores patients’ preferences and intuitive clinical assessment. Third, it applies limited definition of appropriateness (e.g. when the expected health benefits exceed the negative consequences by a sufficiently wide margin (Brook et al, 1986), which does not
take into account resources or the individuality of patients. It also does not make explicit
the risks and benefits that panellists take into account or ignore when making their
judgements. This latter, makes it difficult for users of the appropriateness ratings to
understand their meaning, therefore, hinders judging whether the criteria are suitable in
other settings (Bowling, 2002).

3.1.5 *Iterated Consensus Rating Procedures:* This method involves basing the
evaluation criteria on the effect of guidelines on the outcome of care as rated by expert
panels and professionals. It involves sending mail questionnaires to participants to
evaluate criteria, which takes place privately. Then the panel meets, interacts and
explicitly aggregates their opinions. Unlike the Rand method, this method does not
involve formal feedback of panel choices (Campbell et al, 2003). Iterated consensus has
been applied to develop consensus guidelines for the management of common
conditions in general practice (Steven et al, 1996).

3.2 Analysis of Consensus Methods:
Consensus analysis initially involves summarising the results of the panel agreement
with the criteria (rated on ordinal scale) by using the median and measures of dispersion
(Bowling, 2002; Hunter et al, 1994; Brook et al, 1986). The median is preferred to the
mean, because it is more robust to the effect of outliers (Bowling, 2002). Moreover,
both the mean and standard deviation treat intervals on ordinal scale as equal, which is
not the case, because the risk-benefit levels for each point on the scale are not specified
(Brook et al, 1986). Consensus can also be established by taking the majority of
opinions. To resolve disagreement among panel members, it has been suggested to
continue rounds until consensus is reached or responses diminish. However, this most
probably means exceeding 2-3 rounds, which would make the process tedious and
lengthy. Alternatively, a gold standard could be established if disagreement sustains.
Sometimes, deviation in experts' feedback and opinions was considered as more than
one acceptable option of a standard (Vanderpump et al, 1996). This latter possibility is
often encountered in the management of CVD, where several drug regimens can be used
to achieve therapy goals.
3.3 Limitations of Consensus Methods:
Consensus methods are subject to selection bias of the panel members, who may not be representative of the target population or experts in the subject in question (Bowling, 2002; Jones and Hunter, 1995; Hunter et al, 1994). Moreover, existence of consensus does not mean that consensus views are correct. The process involves the danger of collective ignorance rather than wisdom. Thus, it should not replace rigorous scientific reviews of research (Jones and Hunter, 1995; Hunter et al, 1994). There is a debate about the validity and reliability of consensus methods. Ratings by panellists are dependent on their opinions and the appropriateness definitions used (Hunter et al, 1994). Yet, it is not known how far the stated opinions correspond to the actual practice.

3.4 Credibility and Validity of Consensus:
To establish credibility and validity of the consensus findings, it is recommended to base decisions on empirical data, judgment and experience (Jones and Hunter, 1995; Fink et al, 1984), and to have panel members who are qualified and representative of their profession (Bowling, 2002; Jones and Hunter, 1995; Hicks, 1994; Brook et al, 1986; Fink et al, 1984). Furthermore, to identify the level or type of consensus in advance (Fink et al, 1984) and to match the results of consensus methods to observable events, otherwise it would not be possible to assure they are sound (Bowling, 2002; Jones and Hunter, 1995).

II. Peer Review of Practice:
Peer review could be implemented to assure the quality of drug utilisation processes. To improve the validity of this method, the review should be explicit and based on well-defined standards (Kupperwasser, 1996). Alternatively, peer review was used in DUE studies to validate findings of the assessment of prescribing appropriateness. Reid et al (2001) assessed the quality of prescribing in secondary prevention post MI. Then had 10% of the cases peer reviewed by a cardiology consultant for the validation of the results. Again, well-defined standards should be used to assure the reliability and validity of the validation process.
III. Medication Appropriateness Index (MAI):

MAI (developed by Hanlon et al, 1992) is a scale to evaluate the appropriateness of drug prescribing in terms of 10 key criteria, namely; indication, effectiveness, dosage, directions, practicality, drug-drug interaction, drug-disease interaction, duplication, duration and expensiveness. Each of these criteria is worded as a question. A drug is rated on a 3-point scale for each criterion (A= appropriate, B= marginally appropriate, C= inappropriate) with the support of an explicit definition of each criterion and instructions for use. A score is given for each of the 10 criteria, whose summation yields an overall score, which ranges from 0 (most appropriate) to 18 (most inappropriate). In Hanlon et al (1996) study the MAI was used to evaluate the appropriateness of prescribing in elderly patients, as a means of assessing the impact of a clinical pharmacist's interventions on drug use. Hajjar et al (2005) also used the MAI to assess unnecessary drug use at hospital discharge in elderly patients. Among the limitations of this method is that the evaluation of drug prescribing is implicit, unlike the case in DUE where explicit standards or guidelines are used. Therefore, training before using the MAI is essential. Moreover, the tool is limited to evaluating prescribing and not other components of drug utilisation, e.g. administration or monitoring. It also does not measure some components of drug prescribing such as under-treatment, allergy, and suboptimal choice of therapy (Murray, 1997; Fitzgerald et al, 1997; Schmader et al, 1997).

B) Drug Use Evaluation Study Designs:

1. Descriptive Studies:

As the title indicates, these studies involve describing drug use to identify ongoing practices. Examples of such design are the study by Jackevicius et al (2005), which described the in-hospital use of fibrinolytics and the discharge use of CV medication in myocardial infarction patients. Similarly, the study by Yusuff and Balogun (2005), which described the drug use patterns in hypertensive patients.
2. Comparative studies:
Several studies deployed the evaluation of drug use to compare between the different settings, regions, patient groups, time periods, or performance of health care professionals. The following are some examples on comparative study designs:

2.1 Drug Use in the Different Settings:
Drug use can be compared in the different settings, e.g. wards, hospitals, regions, cities or even countries, hence, give insight into the setting-related factors, which impact the drug use processes. Herlitz et al (2003) compared the use of CV drugs in myocardial infarction patients in two large cities in Sweden and USA. Similarly, Barker et al (2002) compared rates of drug administration errors across states (Georgia vs. Colorado), facility types (hospitals vs. skilled nursing facilities), facility size (small vs. large) and accreditation status (accredited vs non-accredited) of hospitals by the Joint Commission on Accreditation of Healthcare Organisations.

2.2 Before-and-After Studies:
In these studies, DUE has been used to assess the impact of interventions through comparing practice before and after the implementation of the intervention. Both Morgan et al (2001) and Dartnell et al (1995) assessed the impact of academic detailing and the dissemination of guidelines on practice through comparing the use of statins and anticoagulants, respectively, before and after the intervention. The same study design was used by Scott et al (2004) to evaluate the impact of a multi-disciplinary quality improvement program (e.g. guidelines, educational interventions, feedback on performance, clinical pathways, etc.) on the use of CV medication in acute coronary syndrome and congestive heart failure patients.

2.3 Drug Use by Different Health Care Personnel:
An example of implementing DUE to compare between different HCPs is a study conducted by Torella et al (2004) to compare between beta-blockers' use by surgeons and primary physicians. Similarly, Schreiber et al (1995), compared specialists and general doctors in terms of their use of CV drugs and compliance with established
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therapies in unstable angina patients.

3. **Over-time Versus Cross-sectional Design:**

The evaluation of drug use could occur over time, as in Smith et al (2004) study, where the use of CV medication was described in congestive heart failure patients over an eleven-year period, and temporal changes in practice were identified. In contrast, the evaluation of drug use could be cross-sectional, i.e. in a certain point of time, as in many DUE studies (Yusuf and Balogun 2005; Hajjar et al, 2005; Jackevicius et al, 2005; Torella et al, 2004; Filippi et al, 2004).

4. **Retrospective Versus Prospective Design:**

Drug utilisation could be reviewed retrospectively (after the drug has been dispensed), concurrently (during the course of therapy), or prospectively (before therapy is initiated) (Kubacke, 1996). The retrospective design depends on already existing material, is less disruptive to HCPs and patients, allows surveying larger databases and covers greater periods of time. However, the quality of data is determined by the accuracy of the medical records, which may be difficult to judge (Howie, 1989). Despite these drawbacks, the retrospective design is widely used in DUE studies (Suisted et al, 2005; Yusuff and Balogun, 2004; Pearson et al, 2001; Weil and Tu, 2001; McAlister et al, 1999b; Philbin et al, 1996). On the other hand, data in the prospective design are collected with the project objectives in mind, which grants more control over the quality of the data collected. However, usually a smaller amount of material is collected with this design, within a reasonable time, and a workable sample size. Furthermore, it is subject to observer bias, which does not apply to the retrospective design (Howie, 1989). Tandon et al (2004) prospectively evaluated the use of beta-blockers in heart failure patients. Similarly, Albers et al (1996) and Venturini et al (1995), used the prospective design to assess the use of anticoagulants in atrial fibrillation, and CV medication in myocardial infarction patients, respectively.
C) Data Collection Methods Used in DUE Studies:

A variety of methods have been implemented to collect data in drug use research (table, 11). Each of these methods has its advantages and disadvantages. Understanding the cons and pros of each method combined with a sensitivity to the environment and the population studied would enhance the data collection process. The methods commonly used in DUE studies include the following:

1. **Review of Patients’ Records:**
   Having reviewed the literature, the review of patients’ records (medical files, medication charts, prescriptions, discharge summaries, etc.) has been the most commonly used method for data collection in DUE studies (Yusuff and Balogun, 2005; Smith et al, 2004; Pearson et al, 2001; McAlister et al, 1999a; McAlister et al, 1999b; Brigden et al, 1998; Krumholz et al, 1998). This is in spite of its main limitation of incomplete, inaccurate, or illegible documentation (Toal and Walker, 2000; Philbin et al, 1996; Young et al, 1995; Howie, 1989), which could undermine the quality of the collected data. Nonetheless, Bowling (2002) argued that medical records are a better source of information when the amount of information people acquire is limited. Also, in cases where recall and memory bias apply.

2. **Questionnaires:**
   Questionnaires have been also used in data collection in DUE studies. Torella et al (2004) used postal questionnaires to describe beta-blockers’ use by surgeons and general practitioners. Similarly, Irving et al (2000) sent questionnaires to patients to enquire on their aspirin therapy, smoking status, blood pressure control, cholesterol concentrations and treatment. The questionnaires could be combined with other data collection methods. An example is the study by Kalra et al (1999), where postal questionnaires were used in combination with an audit of patient databases to determine the use and monitoring of ACE-Inhibitors in general practice. Telephone questionnaires are another means of data collection. They were used by Burrell et al (1990) to explore the extent of thrombolytics’ use in hospitals.
Questionnaires have the advantages of being economical, granting ease and consistency in data collection, and allowing the inclusion of large and geographically spread samples. However, the pre-coded response choices used in structured questionnaires may not be adequately comprehensive to represent the respondents’ views. Moreover, the response rate with postal questionnaires is usually lower than with interviews, there is no control over who completes the questionnaire, and the responses can be affected by the order of reading the questions. Furthermore, the questions may not be understood by all respondents, especially in the absence of an investigator to explain (Bowling, 2002). Questionnaires were not perceived as a suitable method to evaluate CV drug use at Jordanian hospitals, because they are inconvenient for in-depth exploration of drug use in individual patients. One more crucial factor regarding the use of postal questionnaires in Jordan, is that the postal system is unreliable and accompanied by many delays and losses. Besides, in an environment that is not research-oriented, low response rates to this method were strongly anticipated.

3. Interviews:
Interviews have been also implemented in drug utilisation studies. For example, Toal and Walker (2000) conducted semi-structured interviews in combination with patient record review to study physicians’ prescribing practices in heart failure. The same combination of methods was used by Brigden et al (1998) to investigate the incidence and clinical outcome of anticoagulants’ overuse in outpatients.

4. Observation of Drug Utilisation Processes:
This method has commonly been implemented to assess drug handling and administration. For example, Barker et al (2002) and Taxis and Barber (2004) used observation to assess the rate of medication administration errors (Taxis and Barber, 2004; Barker et al, 2002). Observation can be undisguised, where the study objectives are explained to the observed people (Tissot et al, 2003; Barker et al, 2002). Alternatively, it can be disguised, where the objectives remain undeclared (Taxis and Barber, 2004; Van den Bemt et al, 2002). In all of these studies, an observer watched and wrote down what nurses did during the preparation and administration of drugs.
major concern with this method is the effect of the observer’s presence on the behaviour of the observed, which could weaken the validity of the results. However, it was argued that when nurses were doing familiar jobs and the observers were not obstructive or judgmental, it usually mitigated the effect of the observer and subjects soon returned to their normal behaviour pattern.

**Implications of This Chapter:**

The review of the different DUE methods guided the designing of this project to evaluate CV drug use at Jordanian hospitals. Since, there were no local guidelines or hospital formularies available at hospitals, which could be used to assess practice, DUE criteria had to be developed. The Rand method was perceived as the most suitable for the objectives of the project. It was chosen because it allows using the evidence available in the literature on the appropriate use of CV medication, in combination with experts’ opinions, which is imperative to assure the applicability of the DUE criteria to the Jordanian settings. However, some modifications to this method will be undertaken to minimise its limitations and enhance the validity of the developed DUE criteria. For instance, the DUE criteria will be based on evidence-based rigorously established guidelines, rather than the literature review to eliminate unsystematic reviews. Many guidelines, combine thorough review of evidence with experts opinions, which will establish the appropriateness of the DUE criteria. A panel of cardiology experts from Jordan will be asked to assess the criteria in terms of their applicability and acceptability to evaluate local practice, hence, tailor the criteria to the Jordanian settings. This will overcome the drawback of guidelines of not meeting setting-specific needs. To resolve any ambiguity in developing the criteria, the experts will be asked to clearly state their rationale during assessment. More detail on the rounds for establishing consensus among panel members and the application of criteria to assess CV drug usage will be presented in the methods section in chapters five and six.

The Delphi and expert panel techniques were not chosen, primarily because of how the criteria were developed in these methods, i.e. implicitly by each panel member, which raises concerns on the validity and reliability of the developed criteria. Hence, these
techniques were not used to evade such concerns, especially that evidence-based data on the management of CVD are already established in the literature. Moreover, the questionnaires usually used in these techniques will be inconveniently long if they are to include all the aspects of drug use intended for assessment in this project. This is in addition to the previously stated concerns about the reliability of the postal systems in Jordan, which discourage the use of postal questionnaires. On the other hand, the MAI was not used because the project aims at evaluating CV drug monitoring and follow up of patients, besides prescribing, which is beyond the scope of the MAI.

The next chapter will present a descriptive study to explore the CV drug use processes at Jordanian hospitals. Since no data on this subject were available in the literature, it was imperative to establish a baseline on the ongoing prescribing and monitoring practices in cardiac patients, before proceeding with the evaluation of drug use. This is to further support the planning of the project.
Chapter Four:

Description of Drug Utilisation in Cardiac Diseases at Jordanian Hospitals.

Introduction:
In part one of the thesis, an overall picture of the health status and infrastructure in Jordan is presented. The continuous rise in health expenditure and limited resources are two of the biggest challenges of the Jordanian health care system. The current situation is most likely to sustain - even to get worse- in the light of the escalating patient demand, shifts towards aging, increase in the burden of chronic diseases and the absence of strategies to effectively rationalise the health spending. There are many reports calling for corrective interventions, and warning about the inevitable consequences of neglecting reform of the current situation. Yet, very few reports exist on the evaluation of the system or the ongoing practices, which is actually delaying the planning and eventually the execution of reform. For instance, the hospital services and the use of pharmaceuticals have been identified as major elements of health spending. Moreover, irrational drug use has been reported in the literature and by health care professionals in the interviews (chapter two). Nonetheless, there are almost no studies on describing or assessing the drug use processes and prescribing habits at hospitals. To fill this gap the project was steered into a more clinical direction, focussing on the evaluation of drug use at Jordanian hospitals.

In this chapter and through the subsequent two chapters a hospital-based study to describe and evaluate CV drug use in cardiac diseases at Jordanian hospitals will be presented. The aim is to investigate the current prescribing practices and identify gaps in drug use, hence, advise on areas for improvement. It will also highlight potential areas for pharmacists’ contribution in cardiac patient care, to extend their role beyond the traditional ones described in chapter two.

This chapter presents a descriptive study of the CV drug prescribing and monitoring practices in cardiac diseases at three Jordanian hospitals.
Aim:
To describe CV drug prescribing and monitoring in cardiac diseases in a MOH, a university and a private hospital in Jordan.

Objectives:
1- To characterise adult patients admitted the under cardiology team to medical wards and CCU at the three hospitals in terms of their number, age, gender and casemix.

2- To describe the prescribing regimes followed in treating cardiac patients (total number of drugs per patient, number and types of cardiovascular (CV) drugs per patient, CV drug dosing, frequency, route of administration, and branded and generic prescribing patterns).

3- To describe the monitoring of CV medication (frequency and type of laboratory investigations, blood pressure, heart rate etc.).

4- To describe the level of documentation of patient information, such as medical and drug history, allergy, weight, blood pressure, heart rate and diagnosis.

Methodology:
1. Sampling and Recruitment:
A five-day period was spent at each of the three hospitals (MOH, university and private) during Jan-Feb 2001. Accessibility to the hospitals was established as previously described in chapter two. All adult patients already hospitalised or newly admitted under the cardiology team to medical wards or CCU, as well as patients referred from other specialities for cardiac consultation were included in the study. The patients were prospectively followed from the first day of contacting their files until their discharge or the end of the 5-day study period, whichever occurred earlier. Several measures were taken to ensure capturing all the cardiac patients:
1- The medical wards and CCU were visited several times a day (more than twice daily at different times of the day) to screen inpatients and capture new admissions.
2- Lists of inpatients on wards and CCU, also admission and discharge notes, were reviewed daily.

3- The assistance of cardiology team members and nurses on wards and CCU was sought to confirm new patients’ admission and discharge, and to locate patients’ files if they were not found. This took place at the private and university hospitals, and the CCU of the MOH hospital. It was not possible at the medical wards of the MOH hospital due to the considerable under-staffing.

4- Computer databases at the university and private hospitals were used to track patients when files were missing. This was not applicable at the MOH hospital, as the system was not computerised. Hence, patient files which could not be found on the ward were considered missing.

5- Patients admitted during weekends were captured in the early morning of the next working day. It was unlikely that these patients would be discharged during the weekend, because they needed a consultants’ permission, which usually took place during the week.

2. Data Collection Instruments and Procedures:

Data collection forms were designed (appendix, 3) and field-tested to assure their adequacy and effectiveness in collecting data at the three hospitals. The data collected included:

2.1 The Sample Characteristics:

Patient files were reviewed and data were collected on patient age, gender, weight, past medical history, drug history, present medical complaint, allergies, results of physical examination and diagnosis.

The patient files were reviewed for a second time for 36 patients whose diagnosis was unspecified, i.e. documented as coronary heart diseases without further specification; if it was stable angina, unstable angina or myocardial infarction. Permission was obtained to access the hospitals’ archives and retrieve these files. The files were reviewed by a senior cardiologist at each of the university and the MOH hospitals and a senior cardiology resident at the private hospital to specify diagnosis. This step further
validated the data collection process conducted by the researcher.

2.2 Prescribing Patterns and Therapy Monitoring:
To describe the ongoing prescribing patterns, patient files, physicians’ order notes, medication charts, and CCU bed charts were reviewed on daily basis. Data were collected for individual patients on the types of drugs prescribed and the dosing, frequency, and route of administration of CV medication. Data on the monitoring of CV medication and follow up of patients were collected through daily review of laboratory forms, patient files and progress notes.

The data were considered missing when the patient’s records were not found (could not be located after several daily visits to the ward until the patient discharge or the end of the study). On the other hand, the data were described as not documented, when nothing was stated in any of the patient’s records.

3. Data Processing and Analysis:

3.1 Development of Data Coding Frames:
The data had to be coded for analysis on SPSS software. For this purpose coding frames were prepared for patient age, gender, type of hospital, ward, length of follow up, outcome of stay, and diagnosis (appendix, 4). The development of the coding frame for cardiac diseases to code patients’ diagnosis was preceded by a revision of the pathophysiology of the diseases. Later, the frame was verified and approved by a senior cardiologist from the university hospital. It covered a wide range of cardiac diseases, in addition to all the combinations of concomitant cardiac diseases screened during the study. The coding frames were found to be both effective and practical.

3.2 Description of the Study Sample:
The patient age and gender were described for the whole sample and at each hospital. Patient casemix was classified into different cardiac disease subgroups, highlighting single and concomitant cardiac diseases.
3.3 Description of the Prescribing Patterns:
Lists of all the branded and generic drugs prescribed for the study sample at the three hospitals were prepared. The drugs were classified into cardiovascular and non-cardiovascular, based on the pharmacological classification of the BNF. The BNF was used, because it was comprehensive and covered most of the drugs used at the three study hospitals, especially that there were not any local hospital formularies available, which could have been used.

Drug use was described cross-sectionally, on the last day of contacting the patients’ files. This was to reflect the prescribing practice at the hospitals rather than the drugs received by patients pre-hospitalisation. One exception was the use of fibrinolytics and heparin in myocardial infarction patients, which was described on the first day of contacting the patients’ files, to explore the acute management of the disease.

For all the patients, the total number of drugs and CV drugs concomitantly prescribed per patient were counted. The drug count excluded changes in drug doses. Similarly, drugs given as a stat dose (immediately) followed by continuous infusion were counted as one drug.

The prescribing patterns of CV medication were described in the light of the BNF recommendations. This included describing the use, dosing, frequency and route of administration of the following CV medication: antiplatelets, beta-blockers, ACE-Inhibitors, angiotensin receptor blockers, calcium channel blockers, nitrates, digoxin, diuretics, antiarrhythmics, anticoagulants, fibrinolytics, lipid regulating drugs and trimetazidine.

3.4 Description of the Monitoring of CV Medication:
Monitoring of CV medication (vital signs, frequency and types of laboratory investigations) was also described in the light of the BNF recommendations (table, 12). This involved describing the monitoring of blood pressure, heart rate, renal function tests, liver function tests, electrolytes (sodium and potassium), lipid profile, and haematology indices (e.g. INR, aPTT, complete blood count). Therapy monitoring was
described in patients contacted for more than one day; from the day of contacting the patients’ files until the patients’ discharge or the end of the 5-day data collection period. The analysis involved laboratory tests done during this period. An exception was laboratory investigations recommended by the BNF before the inception of the medication e.g. lipid profile prior to anti-lipid therapy and renal function before ACE-Inhibitors (as shown in table, 12). These tests were included in the data analysis even if they were done out of the period of follow up of patients. In contrast, the analysis excluded laboratory tests, which arrived after drug discontinuation, because it would result in over-estimation of the frequency of laboratory tests (tests done for drugs not prescribed).

Table (12): The BNF Recommendations on Monitoring CV Medication:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monitoring measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>Potassium level and renal function (serum creatinine).*</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Sodium and potassium levels. Renal function and blood pressure*</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>Sodium and potassium levels. Blood pressure. Renal function before and during treatment.</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Blood pressure and heart rate.*</td>
</tr>
<tr>
<td>Nitrates and CCB</td>
<td>Blood pressure.*</td>
</tr>
<tr>
<td>Heparin</td>
<td>aPTT on daily basis (no monitoring is needed for prophylactic regimens of 5000 IU SC b.d. or t.d.s.).</td>
</tr>
<tr>
<td>Warfarin</td>
<td>INR.*</td>
</tr>
<tr>
<td>Lipid-lowering therapy</td>
<td>Fasting lipid profile (LDL, HDL, cholesterol and TG) and liver function tests (AST, ALT) before therapy.</td>
</tr>
<tr>
<td>Tirofiban</td>
<td>Platelet count and haemoglobin before treatment, 2-6 hours after starting drug then once daily.</td>
</tr>
</tbody>
</table>

ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, b.d.: twice daily, t.d.s.: three times daily, WBC: white blood cells, RBC: red blood cells.

* Frequency of test is not specified in the BNF.
3.5 Description of the Level of Documentation of Patient Information:

The level of documentation of patient information, such as past medical history, drug history, allergies, weight and diagnosis was described. Data were missing when the patient files could not be found, and not documented when the data were not found in any of the patients' records.

The SPSS 10.0 software was used in the data analysis. Data entry was double-checked to assure its accuracy. Descriptive statistics such as frequencies, mean, and standard deviation were used. Also, non-parametric tests such as the chi-squared, Mann-Whitney and Kruskal-Wallis tests were used to test for statistical significance.

A section on auxiliary findings was included. These were uncovered during the exploration of the hospital settings. Although they were not part of the study objectives, they were seen worth stating, because they indicated deficiencies in patient care, flow of patient information within the system, communication among HCPs, and aspects of drug utilisation other than prescribing, such as drug administration and nurses' handling of drug orders.
Chapter Four

Results:

1. Sample Characteristics:

Ninety eight adult patients were admitted under the cardiology team in the three hospitals (table, 13). These were distributed as 21 (21.4%), 29 (29.6%), and 48 (49%) patients at the university, private and MOH hospitals, respectively. The mean sample age was 58.9 years old (SD ± 13.4), ranging from 30-88 years old. No significant differences in age were found across the different hospitals. Almost 70% of the patients were ≥45 years old. Males constituted 63.3% of the whole sample, being notably higher than females at the private hospital (p < 0.05).

Table (13): Characteristics of the Study Sample at the Three Hospitals:

<table>
<thead>
<tr>
<th></th>
<th>Type of Hospital</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>University</td>
<td>MOH</td>
</tr>
<tr>
<td>Sample size (%)</td>
<td>21 (21.4)</td>
<td>48 (49)</td>
</tr>
<tr>
<td>Age*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (± SD)</td>
<td>63.4 (±13.7)</td>
<td>58.14 (± 14.0)</td>
</tr>
<tr>
<td>Range</td>
<td>36-84</td>
<td>30-88</td>
</tr>
<tr>
<td>Age group* (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-44 yrs</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>45-64 yrs</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td>≥ 65 yrs</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Gender^ (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>28</td>
</tr>
<tr>
<td>Female</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Ward</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>CCU</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>ICU</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

* Data were missing for 12 patients (1 at university, 6 at MOH and 5 at private hospital).

^ Data were missing for 1 patient at the private hospital.
2. Casemix:
Of the 98 patients, 2 patients were excluded because they had non-cardiac disease diagnosis (a case of severe carotid stenosis and a case of severe hypertension), and for 1 patient data were missing. The final sample included 95 patients, whose casemix is illustrated in table (14). Eighty six patients (90.5%) were diagnosed with cardiac diseases and 9 patients (9.5%) had cardiac signs and symptoms. Of the 9 patients with cardiac signs and symptoms, 4 patients were ruled out as non-cardiac disease cases, 1 patient could not be tracked to identify the results of catheterisation, and 3 patients had no conclusive diagnosis. Half of the sample were diagnosed with single cardiac diseases, whereas 40% had multiple cardiac diseases. The distribution of casemix across the three hospitals is also shown in table (14). Thirty six patients (38%) had cardiac procedures, over half of them were in the private hospital, and none were at the MOH hospital.

Table (14): Patient Casemix at the Three Hospitals:

<table>
<thead>
<tr>
<th>Diagnosis Type of Hospital</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac disease signs/symptoms</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>9 (9.5)</td>
</tr>
<tr>
<td>Single cardiac diseases</td>
<td>11</td>
<td>19</td>
<td>18</td>
<td>48 (50.5)</td>
</tr>
<tr>
<td>CHD</td>
<td>10</td>
<td>14</td>
<td>13</td>
<td>37 (39)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>6 (6.3)</td>
</tr>
<tr>
<td>Valvular diseases</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>6 (6.3)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Diseases of the Pericardium</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Concomitant cardiac diseases</td>
<td>6</td>
<td>24</td>
<td>8</td>
<td>38 (40.0)</td>
</tr>
<tr>
<td>CHD and HF</td>
<td>4</td>
<td>12</td>
<td>6</td>
<td>22 (23.2)</td>
</tr>
<tr>
<td>CHD and others</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>8 (8.4)</td>
</tr>
<tr>
<td>HF and others</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>6 (6.3)</td>
</tr>
<tr>
<td>Others</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>47</td>
<td>27</td>
<td>95 (100.0)</td>
</tr>
<tr>
<td>Cardiac procedures and surgeries[^1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheterisation</td>
<td>10</td>
<td>0</td>
<td>3</td>
<td>13 (36)</td>
</tr>
<tr>
<td>PTCA and/or Stent</td>
<td>7</td>
<td>0</td>
<td>2</td>
<td>9 (25)</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>14 (39)</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>0</td>
<td>19</td>
<td>36 (100)</td>
</tr>
</tbody>
</table>

[^1] Occurred in only 36 patients.
Coronary heart diseases (CHD) were the most common single cardiac diseases, constituting 77% of the diseases (almost 40% of the whole sample), followed by heart failure (HF) in 12% of the sample.

The classification of CHD is shown in figure (10). They primarily comprised unstable angina/Non-ST-segment elevation myocardial infarction (UA/NSTEMI) in 16 patients (43.2%), myocardial infarction (MI) in 10 patients (27%) and stable angina (SA) in 9 patients (24%). A specific diagnosis of CHD could not be identified in 2 patients (5.4%).

Furthermore, CHD and HF were the most common coexisting cardiac diseases. They were diagnosed in 22 patients, constituting 58% of multiple cardiac diseases (23% of the whole sample). Out of the 22 patients, 16 had a specific diagnosis of CHD (SA/HF in 10, and UA/HF in 6). Other combinations of cardiac diseases existed in 16 patients, as shown in figure (11).
2.1 Handling the Cases of Non-specific Diagnosis:

Upon revisiting the patients files for a second time to specify CHD diagnosis in 36 patients, the documentation of diagnosis unspecified was confirmed in 34 files. Nonetheless, the cardiologists could identify a specific diagnosis in 26 patients. These were 9 SA cases, 3 UA, 1 MI, 9 SA/HF, and 4 UA/HF cases. Diagnosis could not be specified in 8 patients due to poor documentation of patient data.

3. Drug Prescribing Patterns:

3.1 Branded versus Generic Prescribing Patterns:

During the study period (5 days), 71, 73 and 98 drugs were prescribed for cardiac patients at the university, the MOH and the private hospital, respectively. Branded prescribing constituted 72%, 80% and 87% of the drugs prescribed at the university, the MOH and the private hospital, respectively. Brands of the CV drugs prescribed at the three hospitals are shown in table (15). A notably higher number of brands were available at the private hospital compared to the other two hospitals. Some of the brands were not listed in the BNF. In contrast, only few drugs were prescribed using generic names, as illustrated in table (16). For some drugs, a mixed branded and generic prescribing practice was noticed, such as digoxin at the MOH hospital, amiodarone at the university hospital, isosorbide dinitrate and digoxin at the private hospital.
Table (15): CV Drug Brands Prescribed at the Study Hospitals:

<table>
<thead>
<tr>
<th>Pharmacological Class</th>
<th>Brand: generic name</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-Inhibitors</td>
<td>Capoten: captopril</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Angiotic*: enalapril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staril: fosinopril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enapril*: enalapril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acuilet: quinapril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coversyl: perindopril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasce: cilazapril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zestril: lisinopril</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiotensin-II receptor antagonists</td>
<td>Blopress: candesartan</td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs</td>
<td>Micardis: telmisartan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-ischemic, anti-anginal</td>
<td>Cordarone X: amiodarone</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Anti-platelets</td>
<td>Vastarel*: trimetazidine</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Anti-platelets</td>
<td>Aspirin: ASA</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Ascriptin*: ASA</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baby Aspirin: ASA</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bufferin: ASA</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlid: ticlopidine</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aggrastat: tirofiban</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plavix: clopidogrel</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persantin: dipyridamole</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blocking drugs</td>
<td>Hypoten: atenolol</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Tenormine: atenolol</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inderal: propranolol</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilatrend *: Carvedilol</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopresor: metoprolol</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visken: pindolol</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>Adalat: nifedipine</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Dilzem: diltiazem</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tildiem: diltiazem</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowvase*: amlodipine</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norvase*: amlodipine</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>Lanoxin: digoxin</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Fibrinolytic drugs</td>
<td>Actilyse: alteplase</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMWH</td>
<td>Clexane: enoxaparin</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Innohep: tinzaparin</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Troparin*: certoparin</td>
<td>√</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASA: Acetyl Salicylic acid (Aspirin). LMWH: Low Molecular Weight Heparin.
Table (15): Continued.

<table>
<thead>
<tr>
<th>Pharmacological Class</th>
<th>Brand: generic name</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid regulating drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>Sivacor*: simvastatin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Zocor: simvastatin</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lescol: fluvastatin</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Lipitor: atorvastatin</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Lipostat: pravastatin</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Fibrates</td>
<td>Lopid: gemfibrozil</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lipo-Merz*: etofibrate</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>Larix: furosemide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Burinex: bumetamide</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td>Aldactone: spironolactone</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Potassium-sparing with thiazide</td>
<td>Moduretic: Co-amilozide</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>Nitrocin: GTN</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Tridil*: GTN</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nitroderm TTS*: GTN</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Isordil ISDN</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>IsokeI: ISDN</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Mono Mack *: ISMN</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

* Not stated in the BNF.

ISMN: Isosorbide mononitrate.

Table (16): CV Drugs Prescribed by Generic Name at the Study Hospitals:

<table>
<thead>
<tr>
<th>Pharmacological Class</th>
<th>Generic name</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac glycosides</td>
<td>Digoxin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Fibrinolytic</td>
<td>Streptokinase</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Inotropic sympathomimetic</td>
<td>Dopamine</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Dobutamine</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>Warfarin</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Parenteral anticoagulants</td>
<td>Heparin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs</td>
<td>Amiodarone</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>ISDN</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>
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3.2 Number of Prescribed Drugs:
The total number of drugs prescribed per patient across all disease groups was highest at
the university hospital (table, 17). However, this was only significant when compared to
the MOH hospital (p ≤ 0.005), but not the private hospital. At the same time, no
significant difference was found between the private and the MOH hospital. The
average number of drugs prescribed per patient in the different disease groups is shown
in table (17). On the other hand, the number of CV drugs prescribed per patient was
significantly less at the private hospital compared to the other two hospitals (p < 0.05)
(table, 18). Table (18) also shows the number of CV drugs prescribed per patients at the
different disease groups. Testing for significant differences in the number of drugs
between the disease groups was not possible due to the small sample size in each group.

Table (17): Number of Drugs Prescribed Per Patient in Each Disease Group:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td>13.5 ± 0.71</td>
<td>7.0 *</td>
<td>7.83 ± 1.33</td>
</tr>
<tr>
<td>SA</td>
<td>6.50 ± 2.43</td>
<td>6.75 ± 0.96</td>
<td>6.8 ± 2.17</td>
</tr>
<tr>
<td>UA/NSTEMI</td>
<td>15.0 *</td>
<td>6.25 ± 2.31</td>
<td>9.0 *</td>
</tr>
<tr>
<td>MI</td>
<td>8.0 *</td>
<td>6.0 ± 2.16</td>
<td>9.0 *</td>
</tr>
<tr>
<td>HF</td>
<td>9.5 ± 0.58</td>
<td>7.75 ± 2.86</td>
<td>8.0 ± 2.19</td>
</tr>
<tr>
<td>Concomitant CAD/ HF</td>
<td>10.2 ± 3.35</td>
<td>6.47 ± 2.26</td>
<td>5.75 ± 3.50</td>
</tr>
<tr>
<td>Others</td>
<td>9.37 ± 3.30</td>
<td>6.78 ± 2.33</td>
<td>7.32 ± 2.15</td>
</tr>
<tr>
<td>Across all conditions †</td>
<td>4 - 15</td>
<td>1 - 14</td>
<td>2 - 11</td>
</tr>
<tr>
<td>Range</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Only one case existed in the disease group. † Data were available for 88 patients.
Table (18): Number of CV Drugs Prescribed Per Patient in Each Disease Group:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>CV drugs prescribed /patient (x ± SD)</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>x ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA</td>
<td>7.50 ± 2.12</td>
<td>6.0</td>
<td></td>
<td>4.33 ± 1.86</td>
</tr>
<tr>
<td>UA</td>
<td>4.67 ± 1.63</td>
<td>5.75 ± 0.5</td>
<td>5.0 ± 2.12</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>10.0 *</td>
<td>5.38 ± 1.92</td>
<td>6.0 *</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>6.0 *</td>
<td>5.0 ± 2.16</td>
<td></td>
<td>4.0 *</td>
</tr>
<tr>
<td>Concomitant CAD/ HF</td>
<td>7.25 ± 0.5</td>
<td>6.0 ± 1.54</td>
<td></td>
<td>4.67 ± 2.5</td>
</tr>
<tr>
<td>Others</td>
<td>4.6 ± 2.3</td>
<td>5.07 ± 2.05</td>
<td>3.0 ± 1.15</td>
<td></td>
</tr>
<tr>
<td>Total sample †</td>
<td>5.84 ± 2.19</td>
<td>5.44 ± 1.77</td>
<td></td>
<td>4.36 ± 1.89</td>
</tr>
<tr>
<td>Range</td>
<td>1 - 10</td>
<td>0 - 9</td>
<td></td>
<td>1 - 8</td>
</tr>
</tbody>
</table>

* Only one case existed in the disease group. † Data were available for 88 patients.

3.3 Types and Prescribing Patterns of CV Drugs:
A full range of the CV drugs stated in the BNF were used at the three hospitals. Tables (15 and 16) list the types of CV drugs used at the three hospitals during the study period. At least one agent from each of the pharmacological groups listed in the BNF was used at the three hospitals. One exception was angiotensin receptor blockers, which were not used at the university hospital.

Data on the prescribing patterns were available for 92 patients, and missing for 3 patients. The prescribing patterns were described against the BNF in 78 out of the 92 patients. The remaining 12 patients had their prescribing patterns described separately for more accurate presentation of the data. This is because 9 out of the 12 patients had cardiac signs and symptoms only, for which the BNF had no clear recommendations on their management. The remaining 5 patients (out of 12) were of miscellaneous casemix, and their therapy options were not adequately addressed by the BNF, e.g. valvular diseases and cardiomyopathy. Therefore, the prescribing patterns in these patients were described independent of the BNF recommendations. Further detail on the prescribing patterns used in the different cardiac disease groups is shown in figure (12).
• Antiplatelets: The BNF recommended the use of antiplatelets in CHD patients. They were prescribed in 59 (89%) out of 66 CHD patients. Figure 12 (a, b, c, e, f) shows the frequency of prescribing antiplatelets in the different CHD subgroups. Aspirin was the most commonly used antiplatelet, which was prescribed in 56 (84%) of the patients, ticlopidine was prescribed in 12 (18%) patients, tirofiban in 2 (3%) patients, clopidogrel and dipyridamole each in 1 (1.5%) patient.

• Beta-blockers, ACE-Inhibitors, and Angiotensin receptor blockers: According to the BNF, beta-blockers and ACE-Inhibitors were recommended in CHD and HF patients. They were prescribed in 41 (52%) and 42 (54%) out of 78 patients with CHD and/or HF, respectively. The frequency of prescribing both drugs in the different cardiac disease subgroups is shown in figure 12 (a, b, c, d, e, f, g). Angiotensin receptor blockers, were recommended by the BNF as an alternative to ACE-Inhibitors. They were prescribed in 3 (3.8%) out of 78 patients. These were a case of SA, a case of CHD/HF, and a case of HF cardiomyopathy.

• Nitrates: Nitrates in the BNF were indicated in CHD and HF patients. However, they were recommended in combination with hydralazine in HF patients. Nitrates were prescribed in 65 (83%) out of 78 patients with CHD and/or HF. They were not combined with hydralazine in any of the 12 HF patients (figure 12: d, g). The frequency of prescribing nitrates in the different cardiac disease subgroups is illustrated in figure 12 (a, b, c, d, e, f, g).

• Lipid regulating drugs: The BNF recommended lipid lowering therapy in all CHD patients. They were prescribed in 16 (24%) out of 66 CHD patients. The frequency of their prescribing across the different cardiac disease subgroups is shown in figure 12 (a, b, c, e, f).

• Diuretics: Diuretics were recommended by the BNF in HF patients. They were prescribed in 25 (73%) out of 34 HF patients (figure, 12: d, e, g). Diuretics were also prescribed for 2 CHD patients, which did not conform to the BNF recommendations.
Cardiac glycosides: The BNF recommended digoxin in HF and arrhythmias. It was prescribed in 21 (62%) of 34 patients with HF (figure 12: d, e, g). Additionally, digoxin was prescribed in 3 patients with concomitant cardiac diseases (figure, 12: f); which included 1 case of CHD and arrhythmia, 1 case of CHD and cardiac arrest, and 1 case of CHD and aneurysm. The use of digoxin in the two latter cases did not conform to the BNF.

Calcium channel blocker: CCB were indicated in angina (stable and unstable) and HF patients. They were prescribed in 9 (13%) out of 68 angina and/or HF patients (figure, 12: a, b, d, e).

Anticoagulant drugs: heparin and LMWH were recommended by the BNF in unstable angina and myocardial infarction. However, they were recommended in a variety of other indications (e.g. surgery, deep vein thrombosis, etc.), thus, their use was described in all the 78 CHD and/or HF patients. Heparin and LMWH were prescribed in 36 (46%) and 7 (9%) patients out of the 78 patients, respectively. The frequency of prescribing both drugs at the different cardiac disease subgroups is illustrated in figure 12 (a, b, c, d, e, f, g) for heparin, and in figure 12 (b, c, e, f) for LMWH. For the same above reason, the use of warfarin was described in the 78 CHD and/or HF patients. It was prescribed in 14 (18%) patients (not shown in figure, 12).

Fibrinolytic drugs: the use of fibrinolytic drugs was recommended by the BNF in the acute management of myocardial infarction. Fibrinolytics were prescribed in 5 out of 10 acute MI patients (not shown in figure, 12).

Trimetazidine (anti-ischemic agent): The BNF does not state indications for the use of trimetazidine. It was prescribed in 3 patients with CHD. These are shown in figure 12 (a, b, c).
• Antiarrhythmic drugs: These were prescribed in 8 (10%) out of 78 CHD and/or HF patients (figure 12: d, e, f, g).

• Miscellaneous: The management of 2 cases of valvular diseases comprised a loop diuretic, digoxin, ACE-Inhibitors, and heparin in one case, and a loop diuretic and digoxin in the second case. The management of one arrhythmia case involved aspirin and a beta-blocker. Additionally, one case of cardiomyopathy was prescribed aspirin, CCB, nitrates and diuretics. Finally, one case of conduction disorders involved ACE-Inhibitors, aspirin, beta-blockers, nitrates, diuretics and heparin.

• The management of the 9 patients with cardiac signs and symptoms is shown in figure 12 (h). It comprised antiplatelets, beta-blockers, heparin, nitrates, CCB and lipid lowering drugs.
Figure (12): Frequency of Prescribing CV Drugs Classified by Casemix:

a) SA Patients (n=9)

b) UA/NSTEMI Patients (n=16)

c) MI Patients (post acute phase, n=10)

d) HF Patients (n=6)

e) CHD/HF Patients (n=22)

f) CHD + others (n=8)

* Data are shown for 77 out of 78 CHD and/or HF patients. The prescribing patterns for 1 CHD patient were not included in the bar charts because the diagnosis was not specified.
**Figure (12): Continued.**

- **g) HF + others (n=6)**
- **h) Cardiac signs and symptoms (n=5)**

The most frequently used CV drugs at each hospital are shown in table (19). These were similar across the three hospitals, except for LMWH.

**Table (19): CV Drugs Most Frequently Prescribed at the Study Hospitals:**

<table>
<thead>
<tr>
<th>CV medication</th>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td>Combination of Aspirin and Ticlopidine</td>
<td>Aspirin</td>
<td>Aspirin</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Atenolol</td>
<td>Atenolol</td>
<td>Atenolol</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>Captopril</td>
<td>Captopril</td>
<td>Lisinopril</td>
</tr>
<tr>
<td>CCB</td>
<td>Diltiazem</td>
<td>Diltiazem</td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Nitrates</td>
<td>ISDN</td>
<td>ISDN</td>
<td>ISDN</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Furosemide</td>
<td>Furosemide</td>
<td>Furosemide</td>
</tr>
<tr>
<td>Lipid-lowering</td>
<td>Simvastatin</td>
<td>Simvastatin</td>
<td>Fluvastatin</td>
</tr>
<tr>
<td>LMWH</td>
<td>Tinzaparin</td>
<td>Certoparin</td>
<td>Enoxaparin</td>
</tr>
</tbody>
</table>
3.4 CV Drug Dosing:

- Antiplatelets: Aspirin dosing complied with the BNF recommended dose in all the patients prescribed the drug. The dosing of dipyridamole, prescribed in one patient only, was below the recommended BNF dose.

- Beta-blockers: dosing complied with the recommended BNF dose in 68% of the patients prescribed beta-blockers. In contrast, it was lower than the recommended dose in 32% of the patients.

- ACE-Inhibitors and Angiotensin receptor blockers: dosing complied with the BNF dose in 97% of the patients prescribed ACE-Inhibitors. It was lower than the recommended dose in 1% of the patients. Dosing of angiotensin receptor blockers complied to the recommended BNF dose in the three patients prescribed the drugs.

- Nitrates: dosing complied with the recommended BNF dose in 84% of patients prescribed nitrates. It was below the recommended BNF dose in 12% of patients, and could not be compared to the BNF in 4% of the patients, due to inadequate documentation of infusion rate.

- Lipid regulating drugs: since statins and fibrates were concomitantly prescribed in 3 patients, the data on their dosing are presented for each drug group separately, for accuracy. Dosing of statins complied with the recommended BNF dose in 29% of the patients prescribed the drug. It was lower than the recommended BNF dose in 64% of the patients, and higher than the BNF dose in 5% of the patients. Dosing of fibrates complied with the BNF recommended dose in 1 out of the 3 patients prescribed the drug. It was below the recommended dose in the second patient and could not be described relative to the BNF in the third patient, because a dose was not stated in the BNF.

- Diuretics: since loop, thiazide, and potassium sparing diuretics were concomitantly prescribed in 6 patients, the data on dosing of each type of diuretic are presented
separately for accuracy. Dosing of loop diuretics complied with the recommended BNF dose in all the patients prescribed the drugs. Dosing of spironolactone was above the recommended BNF dose in 2 out of the 4 patients prescribed the drug. Dosing of thiazides complied with the recommended BNF dose in 2 out of the 3 patients prescribed the drugs. Whereas it could not be described relative to the BNF in the third patient, because a dose was not stated in the BNF.

- Cardiac Glycosides: dosing of digoxin complied with the BNF recommended dose in all the patients prescribed the drug.

- Calcium channel blockers: dosing of CCB complied with the BNF recommended dose in 75% of the patients. It was below the BNF dose in 8% of the patients, and could not be described relative to the BNF in 8% of the patients, because frequency of dosing was not documented.

- Fibrinolytics: dosing of fibrinolytics complied with the BNF recommended dose in all the patients prescribed the drugs.

- Antiarrhythmic drugs: dosing of antiarrhythmics complied with the BNF recommended dose in 75% of the patients, whereas it was higher than the BNF dose in 25% of the patients.

The dosing of some drugs could not be described relative to the BNF recommendations. These included:

- Trimetazidine, hydrochlorothiazide, tinzaparin and etofibrate, because there were no recommended doses stated in the BNF for these drugs.

- Heparin and LMWH, because the BNF doses were stated in units of kg/hr and mg/kg, respectively. Whereas, the prescribed doses were not expressed in weight units (e.g. heparin prescribed as 5000 IU q. 4 hours), and the information on patient weight was not available, which precluded comparing doses to the BNF.

- Tirofiban, because the prescribed doses were not specified (the quantity of drug rather
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than infusion rate was documented e.g. 50 ml in 200 ml distilled water).

More information is available in appendix (5) on the CV drug dosing regimens used in the three study hospitals.

4. Therapy Monitoring:
CV drug monitoring was described for 92 patients, as shown below:

• Digoxin: The potassium level was monitored in 12 (44%) out of 27 patients prescribed digoxin. Whereas renal function, as indicated by creatinine level, was monitored in 11 (40%) out of 27 patients. Data were missing for 3 patients.

• ACE-Inhibitors: Sodium and potassium levels were monitored in 27 (61%) and 26 (59%) patients out of 44 patients prescribed ACE-Inhibitors, respectively. Creatinine level was monitored in 6 (14%) out of the 44 patients before the inception of ACE-Inhibitor therapy, in 11 (25%) patients at the time of prescribing the drugs, and in 21 (48%) patients during therapy. Data on therapy monitoring were missing for 11 (25%) patients.

• Diuretics: Sodium and potassium serum levels were each checked in 15 (48%) patients out of 31 patients prescribed diuretics. Data were missing for 6 (19%) patients. The serum creatinine level was monitored in 15 (48%) patients out of the 31 patients, and data were missing for 5 (16%) patients.

• Heparin: Out of the 41 patients prescribed heparin, 8 patients were prescribed a low subcutaneous heparin dose (5000 IU b.d. or t.d.s.), for which monitoring was not recommended by the BNF. Out of the remaining 33 patients, whose heparin regimen should have been monitored as recommended by the BNF, 6 patients (18%) had aPTT monitored (table, 20). However, 1 out of the 6 patients had aPTT monitored on daily basis as recommended by the BNF. As presented in table (20), 1 out of the 14 patients followed up for 1 day, had aPTT monitored on that day. None of the patients followed up for more than one day had heparin therapy monitored on daily basis. For example, 3
out of the 17 patients followed up for 2-3 days had aPTT monitored for 1 day. Twenty six (79%) out of the 33 patients eligible for heparin monitoring did not have aPTT monitored anytime during their follow up period. Data were missing for 1 patient.

<table>
<thead>
<tr>
<th>LOF (days)</th>
<th>Total number of patients</th>
<th>aPTT monitored in (patients)</th>
<th>Frequency of monitoring aPTT (days)</th>
<th>aPTT not monitored in (patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>14</td>
<td>1</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>33**</td>
<td>6</td>
<td>--</td>
<td>26</td>
</tr>
</tbody>
</table>

LOF: Length of follow up of patients. * Data were missing for 1 patient. ** patients whose heparin therapy is recommended by the BNF for monitoring (8 out of the 41 patients prescribed heparin, did not require monitoring).

- Warfarin: INR was not monitored in 7 (50%) out of the 14 patients prescribed warfarin, in contrast to the BNF recommendation. Two out of the remaining 7 patients had PT monitored instead of INR, whereas therapy was not monitored in the rest of the 5 patients.

- Lipid-lowering drugs: A fasting lipid profile was obtained in 8 (44%) patients out of the 18 patients prescribed a lipid lowering drug. However, in 3 out of the 8 patients the profile was done after the inception of therapy, and in 4 patients it was incomplete, where HDL and LDL were not measured, each in 2 patients. Liver transaminases (ALT and AST) were monitored in 3 patients and AST only was monitored in 7 patients. No monitoring was done in 8 patients.

- Antiplatelets: Ticlopidine and Tirofiban: 8 (57%) out of the 14 patients prescribed ticlopidine had complete blood count (CBC) monitored as recommended in the BNF.
patients. In almost all the 8 patients the monitoring of CBC was incomplete i.e. one or more indicator was not measured e.g. WBC, RBC and/or platelets. The monitoring in 7 out of the 8 patients was done either before or on the same day of starting ticlopidine, whereas it could not be described in 1 patient due to inadequate information. As for tirofiban; 1 out of the 2 patients prescribed the drug had platelet count and haemoglobin monitored on the same day of starting therapy. However, monitoring was not on daily basis as recommended. Data were missing for the second patient.

5. Documentation of Patient Information:
Data on the documentation of patient information was described in 96 patients.

• Blood pressure and heart rate: data on the documentation of both variables were available for 81 patients, and missing for 15 patients. Indications on the monitoring of blood pressure and heart rate existed in 63 (77%) and 67 (83%) patients out of the 81 patients, respectively.

• Weight: data on the documentation of patient weight were available for 82 patients, and missing for 14 patients (table, 21). Weight was documented in 11 (13%) patients out of the 82 patients (8 at private, 2 at MOH and 1 at university). However, 3 out of the 11 patients were documented as obese without specifying weight. Nothing was documented on weight in the rest of 71 (87%) patients.

• Medical and drug history: the documentation of both variables could be described in 84 patients. Data were missing for 12 patients. Medical history (MH) was documented in 82 (97%) of the patients (table, 21). In one patient, MH was documented on second day of hospitalisation rather than on admission. Indications on incompleteness of MH were evident, for instance MH was documented as negative, yet DH indicated therapy of chronic conditions such as heart failure.

While drug history (DH) was documented in 60 (71%) of the patients, documentation was complete in 39 (65%) out of the 60 patients (table, 21). Incomplete documentation in the remaining 21 (35%) patients comprised missing drug name, dose, and/or
frequency. Sometimes, only the therapeutic drug group was documented without specifying the drug name, for example “anti-heart failure therapy”, or “oral hypoglycemic drugs”.

- Patient allergy: data on the documentation of patient allergy were available for 83 patients, and were missing for 13 patients (table, 21). Allergy (whether exists or absent) was documented in 15 (18%) out of 83 patients, and nothing was documented for the rest of the patients. In 1 out of the 15 patients, conflict between the patient file and medication chart was evident, i.e. allergy to paracetamol was indicated in the patient file, whereas “no allergy” was documented in the medication chart.

- Diagnosis: data on the documentation of diagnosis were available for 94 patients, and missing for 2 patients (table, 21). Diagnosis was documented in 91 (97%) out of the 94 patients. However, it was either incomplete in 16 (17%) patients or unspecified in 18 (20%) patients out of the 91 patients, respectively. The latter were all CHD patients, whose diagnosis was not specified; whether SA, UA or MI cases. A final diagnosis was not documented in 3 out of the 94 patients, who had cardiac signs and symptoms.

<table>
<thead>
<tr>
<th>Table (21): Level of Documentation of Patient Information:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Patients</strong></td>
</tr>
<tr>
<td><strong>Complete</strong></td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Medical history</td>
</tr>
<tr>
<td>Drug history</td>
</tr>
<tr>
<td>Allergy</td>
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<tr>
<td>Diagnosis</td>
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</tbody>
</table>

* Data were not documented in patient file. ** Patients files were missing.
6. Auxiliary Findings:

These findings are presented, despite not being related to the study objectives, out of believing in their important implications on drug use and patient care (table, 22). They occurred at varying frequencies, however, most notable was the discrepancy between physicians’ drug orders and nurses’ transcription onto the medication chart.

Table (22): Auxiliary Findings:

**Drug administration errors and documentation in medication chart:**

- Lack of or delay (more than 1 day) in transcribing medication onto medication chart (MC).
- Wrong transcription of prescribing order: wrong dose - frequency - route of administration - rate or duration of infusion - dosing interval.
- Incomplete transcription of prescribing orders: missing drug name, dose, frequency, and/or route of administration (mainly at MOH hospital) - continuous infusion regimen specifications - time of dose administration (before or after meal).
- Dose timing: delay dose or administering it before time (not abiding by dosing interval).
- Dose omission: not giving drug or discontinuing drug without physicians’ order.
- Over dosing: administering un-prescribed doses - continue administering a drug which was discontinued by physician.
- Lack of documentation in MC: administering drugs without signing the MC (personal communication with a nurse administered ISDN, yet did not document it in MC). The same occurred with the time of dose administration - date of therapy inception - date or time of change of therapy.
- Inaccurate or illegible documentation of drugs and dose timing in MC: upon verification with nurses, the MC was signed for drugs which were not yet administered. Similarly, nurses signed the MC for administering drugs prior to the actual date of the prescribing order (MOH), also for administering a dose at 4 pm though the chart was reviewed by researcher at 2 pm - wrong spelling of drug name - discrepancy in documentation between old and new MC.

**Prescribing orders:**

- Discrepancy in prescribing order between patient file and MC (even at university hospital were both are written by physicians).
- Incomplete order: sometimes the dose, route of administration, frequency, and/or date of therapy inception were not specified by physician. Similarly, the rate of infusion for iv drugs.

**Unorganised patient files:** The unorganised patient files makes it time-consuming to understand patient case. The unorganised MC, particularly at the MOH hospital, impedes recognition of the drugs administered, enhances medication errors and hinders auditing.
Table (22): Continued.

<table>
<thead>
<tr>
<th>Discharge summary and medication:</th>
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<tbody>
<tr>
<td>• The patient discharge summary sheet usually has the final diagnosis of case. However, for some patients no final diagnosis was documented anywhere in the files neither in the discharge summary. Furthermore, for some patients the discharge summary was completed post-discharge (in some cases up to 2 weeks), due to the high workload on physicians. Thus, these patients had no final diagnosis neither at the time of or post-discharge.</td>
</tr>
<tr>
<td>• In more than one case, patients did not need the prescribed discharge medication.</td>
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<tr>
<th>Laboratory results:</th>
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<tbody>
<tr>
<td>• Lack of documentation of date and time of laboratory results, predominantly at the MOH hospital, e.g. blood glucose level. Thus, it was not known whether it was a fasting or random blood sugar reading.</td>
</tr>
<tr>
<td>• Normal values are not stated on the MOH Laboratory forms.</td>
</tr>
<tr>
<td>• In several cases, the laboratory tests ordered by physicians were not done, e.g. digoxin level, fasting lipid profile, PT, PTT.</td>
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</tbody>
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<tr>
<th>Patient care:</th>
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</thead>
<tbody>
<tr>
<td>• SOAP reports are only written for critically ill patients (personal communication with a physician at the MOH hospital).</td>
</tr>
<tr>
<td>• Several patient were discharged with inadequate control of hyperglycaemia or HTN.</td>
</tr>
<tr>
<td>• Patients’ reluctance to give feedback on medical service (Personal communication with two patients at the MOH hospital, who asked to be discharged).</td>
</tr>
<tr>
<td>• Communicating patient information during the change of work shifts can involve seriously inadequate and inaccurate information (Personal observation in the MOH hospital).</td>
</tr>
<tr>
<td>• The documentation of follow up of patients and care plan is low in physicians’ and nurses’ notes. Usually it is very brief, illegible, and does not allow full understanding of the patient progress.</td>
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<tr>
<th>Administrative issues:</th>
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<tr>
<td>• Personal communication with a CCU physician at the MOH hospital: The ICU and CCU are overloaded by admission of cases who do not need intensive care.</td>
</tr>
<tr>
<td>• Personal communication with a CCU nurse: Flaws exist in maintaining the CCU drug stock at the MOH hospital.</td>
</tr>
<tr>
<td>• The inadequate number of beds in general wards at the MOH hospital hinders patient transfer and results in longer hospitalisation periods at the CCU.</td>
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</table>
Discussion:

Coding Frame for Cardiac Diseases:
The developed coding frame proved to be effective in coding the patient diagnosis. It showed flexibility in accommodating new combinations of concomitant cardiac diseases, as they were rising during the screening of patients. It is for this reason that the ICD9-CM disease classification system could not be used in coding the patient casemix, because it was not comprehensive to code all the concomitant cardiac diseases included in the sample.

Use of BNF in Describing the CV Drug Use Patterns:
The BNF was used for several reasons. First, it was comprehensive and covered almost all the drugs used in the study hospitals. Second, it was among the drug information sources listed by Jordanian pharmacists in the interviews (chapter two). Furthermore, it was stated in the literature for being used in drug use review activities. Third, as explained earlier, there were no local formularies available, which could have been used to describe the prescribing and monitoring practices. Nonetheless, it has to be said that in some instances, drug prescribing could not be described relative to the BNF, because the latter did not state relevant or adequate information on the drug use. However, this was not considered a limitation, because it applied to a minority of the patients (around 4%) and a few drugs (trimetazidine, etofibrate, tinzaparin).

Patient Characteristics:
Both the sample demography and the prevalence of CHD in this study are in harmony with reports from other Jordanian studies and international reports. Having more male patients of older age conforms with the demography profile of the Jordanian sample in Khoury et al study (1995-96), as well as in developed countries like the US (AHA, 2006) and the UK (BHF, 2005). Similarly, having CHD as the most prevalent, constituting 40% of the study sample, largely resembles their prevalence in the study by Khoury et al (1995-96), which involved 200,000 Jordanian cohort (50% CHD), despite the considerable difference in the sample size between the two studies. This high rate of
Chapter Four

CHD is also comparable to the international patterns of CHD prevalence among other CVD (AHA, 2006; BHF, 2005).

The Study Hospitals:
The setting-related limitations reported by the interviewed health care professionals at the public hospitals (chapter two), such as under-staffing, high workload, unavailability of drugs and equipment were clearly evident, predominantly in the MOH hospital. In contrast, the reported abundance of resources in the private sector was reflected in the much better conditions and less congested environment at the private hospital, compared to the other two public hospitals.

The none existence of cardiac procedures and surgeries in the MOH hospital, unlike the other two hospitals, is attributed to the unavailability of catheterisation laboratories and surgery facilities in the hospital. Patients are referred to other hospitals if cardiac procedures are required.

Branded versus Generic Prescribing:
The prevalent branded prescribing practice at the three hospitals corroborates the reports from the interviews (chapter two) and the literature (WHO, 2003; World Bank, 1997). It is also parallel to the branded prescribing practice reported at primary care level (Otoom et al, 2002a). It further emphasises the strong impact of pharmaceutical promotion on physicians’ practice in all sectors.

The notably higher number of drugs and wider range of brands at the private hospital reflects the previously reported higher availability of resources and generous drug procurement policies (interviews in chapter two and the literature). In contrast, the limited range of drugs at the public hospitals, particularly the MOH hospital, explains what HCPs reported on the unavailability of medicine as one of the factors, which impede practice.

CV Drug Utilisation Patterns at the Study Hospitals:
The number of CV drugs prescribed per patient (average 4-5 drugs) is expected given

-178-
the cardiovascular co-morbidities in 40% of the sample, and that elderly patients (above 64 years old) accounted for one third of the sample. Additionally, many of the patients had hypertension. The higher availability of drugs at the private hospital was not associated with a higher number of drugs per patient compared to the other two hospitals. Interestingly, it was at the university hospital that patients received the highest number of drugs, despite the reports on drug unavailability by the university HCPs in the interviews. This could be explained in the light of the reports on excessive and irrational drug use by the interviewees, however, such assumption can not be made at this stage of the study, also with the small sample size.

The rates of CV drug utilisation in this study are within the range of rates reported in the literature. Drugs particularly in low use included beta-blockers in 52%, ACE-Inhibitors in 54%, and lipid lowering medication in 24% of the sample. However, underuse of CV medication has been reported in several other studies, which does not associate with the substantial evidence established on the benefits of these drugs in CVD, as illustrated in chapter three (section, 1). An audit conducted by Brady et al (2005) on secondary preventive measures in CHD patients indicated low use of beta-blockers in 40%, ACE-Inhibitors in 27% and statin in 49% of the patients. The evaluation of ACE-Inhibitors use in heart failure patients by Pearson et al (2001) showed that only 68% of the patients were discharged on ACE-Inhibitors. The use of digoxin was reported in 32% of heart failure patients (Misiaszek et al, 2005). Another study at three major Australian public hospitals illustrated the under-treatment of CHF, where ACE-Inhibitors were used in 50% of patients, beta-blockers in 22%, loop diuretics in 65%, spironolactone in 15%, digoxin in 24% and ARBs in 8% (Stafford and Radley, 2003). Lower rates of ACE-Inhibitors were found by Mendelson and Aronow (1998) in elderly MI patients (35%), as well as in MI and HF patients (67%). The use of fibrinolytics ranged from 60-70% in MI patients at Jackevicius et al (2005). In the same study, the use of CV medication at discharge included: aspirin 83-88%, beta-blockers 74-89%, ACE-Inhibitors 54-67%, statins 41-53% and calcium channel blockers 21-32%. Higher rates of CV drug use were reported in Pancu and Lee (2003) study, who found the use of beta-blockers in 96% of MI patients. Also, in the study by Ramahi et al (2000), where ACE-Inhibitor use in HF
ranged 87-100%.

It is realised that the description of CV drug patterns did not include allergies and/or contraindications in the analysis, however, this was not meant at this stage of the study, because the purpose was to explore and not to evaluate drug use. These issues will be highlighted in more depth during the evaluation of CV drug use processes, as shown in chapter six.

**Level of Documentation:**
The experience with incomplete and/or ambiguous documentation in patient records in this study is no different from reports from other settings (Toal and Walker, 2000; Philbin et al, 1996; Young et al, 1995; Howie, 1989). Most notable is the prevalent documentation of CHD without stating a specific diagnosis (stable and unstable angina, and myocardial infarction), which raises questions on how the variation in the management of the different CHD is identified. How would low documentation of diagnosis impact the flow of accurate information among HCPs and consequently patient care still needs to be investigated. However, it could be anticipated to introduce serious flaws in patient care in settings like those of the study, in the light of the poor communication among HCPs and the absence of multi-disciplinary team work reported in the interviews.

In the same context, the lack of documentation of weight undermines accurate dose calculations (e.g. heparin, enoxaparin) and hinders monitoring of therapy (e.g. diuretic therapy in HF patients), which is important to determine the success of disease management.

**Limitations:**
Measures taken to minimise the limitation of incompleteness of the medical records, as much as possible, included the referral to several types of patient records to collect the data. Also, collecting the data prospectively rather than retrospectively, which enabled seeking the assistance of the medical staff, whenever possible, to clarify ambiguous or
missing data. Having said that, the very poor condition of medication charts witnessed at the MOH hospital allows advising on the unfeasibility of conducting quality assurance activities (e.g. audit) solely based on the review of medication charts.

The patterns of drug utilisation were not compared between the different disease groups due to the small number of patients in each group, and their unequal distribution between the three hospitals. Yet the sample size was not perceived as a limitation, because the objectives of preliminary description of CV drug use patterns at the study hospitals have been fulfilled.

One of the personal experiences encountered during the study was the discontent expressed by the nurses because the researcher reviewed the medication charts. This was predominantly at the MOH and university hospitals. Although this did not affect the data collection, it made the process less smooth. This discontent may be attributed to the fact that health care personnel are not oriented to research.

Key Points and Implications of This Chapter:

• Coronary heart diseases and/or heart failure are the most prevalent cardiac diseases in the study sample, constituting up to 70% of the patients.
• A full range of the cardiovascular drugs are used at the three hospitals, and variations in drug availability exist across the different settings.
• Rates of CV drug use at the study hospitals are comparable to the rates reported in the literature, however, the appropriateness of practice is not known.
• Dosing of CV medication (for each drug group except anti-lipids) conformed with the recommended BNF dose in at least 70% of the patients. Yet, more investigation is needed to identify the appropriateness of the dosing practice.
• Indications on the inadequate monitoring of medication exist, based on the BNF recommendations.

In the light of the above key points, the evaluation of the appropriateness of CV drug utilisation processes became the focus of the project, to identify gaps in practice and the
potential areas for pharmacists’ contribution in patient care.

In the next chapter, the development of local guidelines (templates) for the use of CV medication in coronary heart diseases and heart failure will be discussed. The guidelines will be used as a tool to assess CV drug utilisation processes at the study hospitals in the following diseases: stable angina, unstable angina/non-ST-segment elevation myocardial infarction, myocardial infarction and heart failure. These diseases were chosen because they were the most prevalent in the study sample.
Chapter Five:

Development of Templates of Drug Use Evaluation (DUE) Criteria for Coronary Heart Diseases (CHD) and Heart Failure (HF).

Introduction:

The previous chapter described the patterns of CV drug utilisation at Jordanian hospitals. However, the appropriateness of the ongoing practices was not investigated. Assuring the appropriate use of CV drugs is a mainstay for the effective management of CVD. The project was directed towards the evaluation of drug use processes for several reasons. First, the reports in the interviews and the literature on irrational use of drugs. Second, the absence of practice guidelines and standardisation of care in all the study hospitals. Third, the aspiration to optimise drug use processes at Jordanian settings. The assessment of drug use will allow the identification of suboptimal practice and proposing recommendations on areas for improvement, as well as the opportunities for pharmacists in patient care. Hence, it will serve the overall objectives of the project described at the beginning of the thesis.

The lack of local practice guidelines or drug use criteria, which could have been used in the assessment of Jordanian prescribing practices, mandated devising a tool for this purpose. This chapter presents the development of templates of explicit DUE criteria for the assessment of CV drug use at Jordanian hospitals, based on international cardiology guidelines. Out of realising the strong ownership of practice by physicians in Jordan, it was very important to get them involved in the development of the templates, and thus gain their support and establish reliability of the templates at the local settings. For this purpose, a panel of cardiologists was invited to participate in the project. The panel undertook the adaptation of the templates to the Jordanian settings, to ensure their applicability in assessing local practices. The templates will be developed for the most prevalent cardiac diseases described in the previous chapter. Namely, the stable angina, unstable angina, myocardial infarction and heart failure diseases. The aim, objectives and methodology of developing the templates are presented below.
Aim:
To develop templates of explicit DUE criteria for the assessment of CV drug use processes in CHD and HF patients at Jordanian hospitals.

Objectives:
1- To review international cardiology guidelines and agree with key Jordanian cardiologists the guidelines to be used in developing the templates.

2- To develop templates of explicit criteria for the evaluation of CV drug use in CHD (stable angina, unstable angina, myocardial infarction), heart failure and concomitant CHD and heart failure patients, based on the agreed cardiology guidelines. The DUE criteria will involve:
- Prescribing of CV medication (indications, choice of drugs, doses, frequency, route of administration and contraindications).
- Therapy monitoring (vital signs and laboratory investigations; e.g. renal and hepatic functions, lipid profile, haematology indices with anticoagulants, digoxin level etc.).
- Following up of patients (therapy outcome).

3- To adapt the templates to the Jordanian settings to assure their validity in assessing drug use at the three study hospitals (university, MOH, and private). This involves:
   a- Review of the templates by a panel of leading cardiology consultants from the three hospitals to assess the applicability and acceptability of the DUE criteria -listed in the templates- in assessing Jordanian practice.
   b- Establish consensus among the panel members on the DUE criteria to be included in the templates.
   c- Describe deviations between the cardiologists’ views (Jordanian clinical practice) and the guideline-derived DUE criteria (international practice).
   d- Confirm with the panel members on the templates of explicit DUE criteria to be used in assessing Jordanian practice at the three study hospitals.
Methodology:

Sampling and Recruitment: The Selection of Cardiologists:
The sample is a purposive one. Senior cardiologists from the three hospitals (university, MOH and private), who were introduced to the study objectives during previous fieldwork, were invited to participate in the project. A panel of three senior cardiology consultants was formed; one from each hospital. All the consultants were prominent practitioners in their hospitals, and the one from the university hospital was the head of the cardiology department. The criteria for selecting the panel members were:

- Opinion leaders, who were capable of influencing the views of other practitioners. The three consultants participated in teaching medical residents, which was previously reported to influence the prescribing practices of doctors (from the interviews in chapter two).
- Long work experience.
- Awareness of the circumstances, resources and limitations of their settings, so they are able to advise on the applicability of the templates at Jordanian hospitals.

The Development of the Templates:

1. Search for Cardiology Guidelines:
Cardiology guidelines were located through:

a) Searching the websites of prominent cardiology societies for guidelines on the management of CHD and HF, such as:

- The American College of Cardiology (ACC).
- The American Heart Association (AHA).
- The European Society of Cardiology (ESC).
- The British Cardiac Society (BCS).
- The Scottish Intercollegiate Guidelines Network (SIGN).
- National Institute of Clinical Excellence (NICE)/National Service Framework for Coronary Heart Diseases (NSF)/Department of Health (DOH).
- National Heart, Lung and Blood Institute/National Cholesterol Education Programme (NCEP).
• The National Heart Foundation of New Zealand.
• The Royal College of Physicians.
• The British Medical Association.
• The American Medical Association.

b) Searching the bibliographies of the literature reviewed on CV drug use evaluation for the guidelines implemented in the evaluation.

c) Discussing with two specialist clinical cardiology pharmacists from a London teaching hospital the clinical guidelines available on the management of CHF and HF.

d) Consulting with the Jordanian cardiologists on the clinical cardiology guidelines, which they use or think as suitable to assess Jordanian practice, whether national or international.

2. The Compilation of the Templates:
Findings from the search for cardiology guidelines were discussed with the study cardiologists. The most up-to-date guidelines published by well-known cardiology bodies were highlighted by the researcher. The cardiologists’ approval of the guidelines to be used in developing the templates to assess Jordanian practice was sought.

The templates were developed using several guidelines, which complemented each other. These included:

• The ACC/AHA guidelines for the management of HF (2001), SA (2002), and UA/NSTEMI (2002), and the ESC guidelines for the management of MI (2003). These were the primary guidelines on which the templates were based.
• The British National Formulary (BNF) was primarily used for recommendations on drug dosing and contraindications.
• The National Cholesterol Education Programme Report (NCEP) on the detection, evaluation and treatment of high blood cholesterol in adults (2002) was used to complement the above guidelines, for recommendations on lipid-
lowering drug therapy.

- The New Zealand guideline on the management of HF (2001) was used to complement the above ACC/AHA guidelines. Similarly, the ACC/AHA guidelines (Ryan et al, 1999) and the NICE guidelines (2001) for the management of MI, were used to complement the ESC guidelines.

The above guidelines were reviewed for criteria on the prescribing and monitoring of CV medication, and the following up of CHD and HF patients during hospitalisation. In some instances, where data on CV drug use were not available in any of the guidelines, the literature (randomised controlled trials and meta-analysis), drug compendium, and drug databases were consulted for evidence. For example, the mode of heparin infusion in acute CHD, or the prophylactic dose of verapamil post MI.

Four templates of explicit DUE criteria for the use CV drugs in the areas of SA, UA/NSTEMI, MI, HF and concomitant CHD/HF were compiled.

3. Structure, Components and Scope of the Templates:
The templates were designed in a guideline format. Every effort was made to keep them concise and manageable to facilitate their review by the cardiologists’ panel. They included:

a) Explicit criteria for prescribing CV medication, which advised on:

- Drug indications.
- Doses, illustrating dose range and adjustment in special patient groups (e.g. elderly, renal or hepatic impairment, patients developing intolerance).
- Duration of therapy.
- Contraindications and clinically significant drug interactions.
- Drugs of choice in a pharmacological group (e.g. selective vs. non-selective beta-blockers, loop vs. thiazide diuretics, immediate vs. slow-release calcium channel blockers etc.), and CV drug combinations, which can be used in disease management.
b) Explicit criteria for CV drug monitoring, which advised on the:
- Monitoring of vital signs such as blood pressure (BP) and heart rate (HR).
- Laboratory investigations such as kidney and liver function tests, blood biochemistry (electrolytes), haematology indices (WBC, platelets, Hgb, PT, PTT, INR), lipid profile, digoxin level in suspected digitalis toxicity, etc.
- Frequency of monitoring therapy for some CV drugs (e.g. daily, weekly), such as heparin, ticlopidine, and lipid-lowering drugs.

c) Explicit criteria for following up of cardiac patients, which advised on the monitoring of therapy outcome, i.e. the relief of ischemic pain in angina patients or HF signs and symptoms. Also the follow up of BP, HR, digoxin toxicity symptoms, and bleeding signs etc.

The templates also advised on public health issues and general measures in cardiac patient care such as smoking cessation, life-style modification, physician activity, and control of hypertension, hyperglycemia and thyroid disorders.

4. Validation and Adaptation of the Templates to the Jordanian Settings:
The appropriateness of the DUE criteria listed in the templates was already inherited by basing them on evidence-based, rigorously developed international guidelines. However, the importance of tailoring the criteria to the Jordanian settings was realised. Therefore, the criteria were reviewed by a panel of senior Jordanian cardiologists to assess their validity for the evaluation of Jordanian practice at the study hospitals. The assessment by the panel of cardiologists and establishing consensus among them on the DUE criteria (templates) took place over several steps, which are explained below.

4.1 Establishing Consensus among Cardiologists on the Templates of DUE Criteria:
The Rand technique was modified and used to establish consensus among the panel members on the criteria to be implemented in the evaluation of CV drug use at the three study hospitals. The process occurred over three rounds, at the end of which, consensus was established among the cardiologists and four templates of explicit DUE criteria for the management of SA, UA/NSTEMI, MI and HF were produced (appendix, 10). Figure (13), shows a flow chart, which depicts the three rounds for further illustration.
Figure (13): Flow Chart of the Development and Validation of the Templates:

First Round

Cardiology Guidelines

Templates of DUE criteria (prepared by the researcher)

Sent to a panel of senior cardiologists

Assessment of the templates to assure validity of the DUE criteria in evaluating Jordanian practice.

Feedback (analyzed and categorized)

All panel agrees with DUE criteria (consensus)

Request clarification of ambiguous criteria

Addition to the templates

Disagreement with the criteria

Second Round

Lists of all the issues raised in round 1 along with anonymous feedback of the panel and copies of the guideline sections relevant to ambiguous or disapproved criteria

Sent to the cardiologists panel

Feedback analyzed and categorized

All panel agrees with DUE criteria (consensus)

Disagreement with the criteria (persisting from round 1)

Issues still Unresolved

Evidence supporting the additions to the templates

Ambiguous feedback

Elaboration on Jordanian setting-specific issues

Third Round

All panel disagrees (consensus)

No consensus

"Jordanian practice"

Use guidelines "Gold standard"

Sent with feedback for re-evaluation

Further evaluation of evidence

Further clarification and resolution

Added to the results section (not part of the final templates)

All panel agrees (consensus)

Final Templates

All issues were resolved by the end of round 3

Chapter Five
4.1.1 The First Round:
The first round commenced with delivering the templates -developed by the researcher- along with covering letters (appendix, 6A) to the three cardiologists in person. The goals and objectives of reviewing the templates were explained to the cardiologist verbally, as well as in the covering letters. Each cardiologist was asked to state his agreement or disagreement with the DUE criteria -derived from the guidelines- and to assess their validity to evaluate practice at his local setting (MOH, university or private hospital). The cardiologists were encouraged to explain their rationale in case of disagreement with the criteria, and to state the reasons, whenever applicable. Reminders were sent, nearly fortnightly, to speed up the feedback process. The cardiologists’ feedback was compared, and the templates were amended to accommodate all their suggestions. Disagreement with the criteria and its rationale were described. Issues which needed further re-assessment were identified and categorised (appendix, 7). Then they were organised into lists (appendix, 8) and sent to each cardiologist, along with the feedback from the rest of the panel (anonymous), on a second round for re-evaluation.

4.1.2 The Second Round:
This round involved assessing the issues unresolved in the first round (appendix, 7). It entailed clarification of ambiguous criteria highlighted by the panel, evaluation of the information added to the templates, and the resolution of disagreement within the panel. Covering letters were prepared (appendix, 6B), summarising the categories of feedback generated from the first round, explaining the goal of re-assessment in the second round, encouraging the cardiologists to reach consensus, and listing the contents of the packages sent to the panel. Each cardiologist was sent lists of the issues raised on each template (appendix, 8), copies of the guidelines corresponding to the criteria in question (whether ambiguous or disapproved criteria), the additions to the templates and the feedback of the other panel members. The copies of the guidelines were included so that all the cardiologists have access to the same information sources when assessing the criteria. The cardiologists were asked to evaluate the added information and, in case of agreement, to state the evidence which supports it. Similarly, they were asked to re-assess the disagreed criteria in the light of the guidelines and the panel feedback, and
justify their assessment. In case disagreement with the criteria persisted, the cardiologists were asked to state alternative practice, along with the evidence supporting it. The reasons of disagreement with the DUE criteria were described in the results section and more thoroughly in appendix (9), as they give more insight into the study settings' conditions.

Feedback from this round was compared and categorised as in the first round. The additions to the templates were incorporated when the majority of the panel agreed on them. The evidence supporting the added information was stated, whenever possible. Disagreement was resolved with unanimous consensus of the panel. If all the cardiologists disagreed with the guideline-derived DUE criteria, then the practice suggested by the panel substituted the guideline recommendations. These represented the “Jordanian practice”. On the other hand, if no consensus was reached, then the guideline criteria were applied as the “gold standard”, unless the different opinions of cardiologists represented several acceptable options of practice. Issues which were not resolved in this round were sent on a third and a final round for further re-evaluation by the panel.

4.1.3 The Third Round:
This round involved the clarification of ambiguous or incomplete feedback from the previous round, the elaboration on the study setting-specific issues, further evaluation of the evidence supporting the added information, the re-evaluation of some of the amendments suggested by the panel, and the resolution of any sustaining disagreement. As in the previous round, lists of the unresolved issues were sent to each cardiologist, along with anonymous feedback of the other panel members. Sometimes verbal communication with the cardiologists (e.g. telephone calls) took place when feedback was delayed. In such case thorough notes of the cardiologists’ comments were taken. The cardiologists’ feedback was analysed and issues were resolved in the same way as explained above. At the end of this round, the finalised templates (appendix, 10) were sent to the cardiologists (for confirmation) and official letters of their approval of the templates were obtained (appendix, 11).
Results:

1. Response Rate of the Cardiologists:
All the cardiologists welcomed participation in the project and expressed willingness to
develop the DUE templates for the assessment of practice at Jordanian hospitals,
especially that local treatment guidelines did not exist. Similarly, feedback was received
from all the cardiologists in all the rounds.

2. Results from the Search for Cardiology Guidelines:
I- The clinical pharmacists from UK suggested the following websites:
- www.druginfozone.nhs.uk.
- www.eguidelines.co.uk.
- www.heartuk.org.uk
- www.sign.ac.uk
Searching the above websites and those of the cardiology societies stated earlier in the
methods section resulted in locating several guidelines, the following were the most
recent ones at the time of search:
- The ACC/AHA guidelines for the management of HF (2001), MI (Ryan et al,
1999), SA (2002), and UA/NSTEMI (2002).
- The ESC guidelines for the management of MI (2003), HF (2001), UA (2000),
and SA (1997).
- The NICE guidelines for the prophylaxis of MI patients (2001), and the
- The National cholesterol education programme (NCEP) report on the detection,
evaluation and treatment of high blood cholesterol in adults (2002).
- The Scottish Intercollegiate Guidelines Network (SIGN) guidelines for:
the management of SA (2001), secondary prevention of CHD following MI
(2000), diagnosis and treatment of HF due to LVSD (1999), and lipids and the
primary prevention of CHD (1999).
II- Searching the bibliographies of the literature on cardiovascular DUE generated the following guidelines:

- ACC/AHA guidelines for the management of HF, MI, SA, and UA.
- DOH national service framework for CHD.
- SIGN guidelines for primary and secondary prevention; for the use of aspirin, statins, beta-blockers and ACE-Inhibitors.
- The British National Formulary.

3. The Selection of the Guidelines:
The discussions with the cardiologists from Jordan resulted in selecting the most recent guidelines by the ACC/AHA and ESC, also the BNF for the development of the templates. Other guidelines such as the New Zealand guidelines for HF (2001) and the NCEP/ATP III report on the evaluation, detection and treatment of high blood Cholesterol (2002) were also approved. Similarly, the referral to the literature (e.g. clinical trials, meta-analysis, books, drug compendium) to complement the guidelines was supported.

4. The Development of the Templates:
4.1 Data obtained from the literature to complement the guidelines:
Eight criteria relevant to CV drug use were extracted from the literature, because they were not available in any of the guidelines. These were all approved by the panel before inclusion in the templates. They are listed in appendix (9: A) for further illustration.
4.2 Results from the validation and adaptation of the templates by the cardiologists

(Establishing consensus):

The feedback of the cardiologists on the assessment of the templates in the three rounds is presented in table (23). Fewer issues were evaluated by the panel as the rounds progressed (the 4 templates in round 1, 47 issues in round 2, and 9 issues in round 3). Consensus was established and the templates were finalised at the end of the third round.

Table (23): Number of Issues Discussed and Types of Cardiologists’ Feedback Generated During Consensus Development:

<table>
<thead>
<tr>
<th>Number of issues</th>
<th>First round</th>
<th>Second round</th>
<th>Third round</th>
</tr>
</thead>
<tbody>
<tr>
<td>The four templates.</td>
<td>47 issues</td>
<td>9 issues</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Types of feedback</th>
<th>First round</th>
<th>Second round</th>
<th>Third round</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement with the templates.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Request of clarification of ambiguous criteria.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elaboration on the Jordanian setting-specific issues.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addition of information to the templates.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disagreement with the criteria, its rationale and alternative practice.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Finalised Templates (all issues were solved by the 3rd round)

Clarification of ambiguous feedback.

In the first round, the cardiologists agreed with all the templates, except for 47 issues (appendix, 7), which needed further assessment. These were classified into the following categories:
1- Requests for clarification of ambiguous DUE criteria (12 issues).

2- Addition of information to the templates (e.g. doses or drug indications) (11 issues).

3- Disagreement with the DUE criteria (derived from guidelines), its rationale and alternative practice (24 issues). All of these were resolved in the subsequent rounds as follows:

1- Ambiguous Criteria and Feedback:
All the ambiguous criteria (12 issues) were clarified in the second round. Similarly, ambiguous cardiologists’ feedback from the second round was resolved in round 3 (2 issues).

2- Additions to the Templates:
Both the second and the third rounds involved the assessment of the information added to the templates and the evidence supporting them (11 issues in round 2, and 3 issues in round 3). All the additions were included in the templates except for three, which were rejected due to inadequate evidence. The additions and their supporting evidence are listed in appendix (9: B) for further detail.

3- Disagreement with the Templates:
The re-assessment of the disagreement within the panel (24 issues in round 2, and 4 issues in round 3), resulted in the resolution of 18 issues (positive consensus). Unanimous disagreement with the guideline criteria (negative consensus) was reached for (5 issues). As a result, the guideline criteria were modified or substituted with the Jordanian practice as shown in table (24). These were incorporated into the templates and referenced as “consensus panel”. Further detail on how the guideline-criteria was amended is included in appendix (9: C).

The modified guideline-derived criteria “Jordanian practice” along with the additions to the templates represent the adaptation of the templates (international guideline-derived criteria) to the Jordanian settings.
Table (24): Modified Guideline Criteria “The Jordanian Practice”:

<table>
<thead>
<tr>
<th>Guideline-derived DUE criteria (before modification)</th>
<th>The modified consensus criteria “Jordanian Practice”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give combination of hydralazine and ISDN if intolerance to ACE-Inhibitors due to hypotension.</td>
<td>Give combination of hydralazine and ISDN very cautiously, in low doses if intolerance to ACE-Inhibitors due to hypotension.</td>
</tr>
</tbody>
</table>

Management of ventricular arrhythmias in HF:
If asymptomatic ➔ Do not treat.
If asymptomatic ➔ Leave to the physician’s discretion.

Management of sinus bradycardia post MI:
If sinus bradycardia accompanied by severe hypotension ➔ Give iv atropine (0.3-0.5 mg, repeated up to 1.5-2 mg).
Give iv atropine at (0.6-1 mg) repeated up to a total of 2 mg or (0.04 mg/kg).

Management of cardiogenic shock post MI:
Give dopamine 2.5-5 mcg/kg/min. Consider additional dobutamine 5-10 mcg/kg/min. Maintain SBP > 90 mmHg.
Give dopamine initially 2.5-5 mcg/kg/min, gradual up-titration to 15-20 mcg/kg/min (until SBP > 90-100 mmHg). If higher doses are required, give norepinephrine infusion 0.02-0.04 mcg/kg/min. Dobutamine (5-10 mcg/kg/min) is preferred if SBP > 90 mmHg. Maintain SBP > 90 mmHg.

Dosing of diltiazem:
Immediate-release: 30-80 mg q.d.s.
Slow-release: 120-320 mg o.d.
Immediate-release: 30-60 mg t.d.s.
Slow-release: 200-300 mg o.d.

On the other hand, the disagreement among the panel members was not resolved for (5 issues). Therefore, the guideline-derived criteria were included in the templates without amendment; as the ‘gold standard’. These are summarised in table (25) along with the deviating opinions of the cardiologists. They are also listed in appendix (9: D), along with the cardiologists’ rationale for disagreement, whenever available, for further illustration.
Table (25): DUE Criteria for Which No Consensus was Reached “Gold Standard” Versus the Deviating Cardiologists’ Opinions:

<table>
<thead>
<tr>
<th>Guideline-derived DUE criteria ‘Gold standard’</th>
<th>Cardiologists’ opinions deviating from the guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heparin use in ACS:</strong></td>
<td>Routine practice at the MOH hospital is 5000 IU iv q.q.h. (obstacles in weighing patients, calculating doses, and obtaining laboratory results of aPTT were reported to impede abiding by the guidelines).</td>
</tr>
<tr>
<td>Weight adjusted regimen: iv bolus: 60-70 U/kg (maximum 5000 U) followed by infusion: 12-15 U/kg/hr (maximum 1000 U/hr), titrated to aPTT 1.5-2.5 times control.</td>
<td></td>
</tr>
<tr>
<td><strong>Use of spironolactone in HF:</strong></td>
<td>Routine practice at the MOH and university hospitals is to use spironolactone in mild-moderate HF cases.</td>
</tr>
<tr>
<td>Drug can not yet be recommended in mild- moderate HF. Reserve for use in severe HF cases.</td>
<td></td>
</tr>
<tr>
<td><strong>Management of ischemic pain in ACS:</strong></td>
<td>Pethidine is routinely prescribed instead of morphine at the MOH hospital.</td>
</tr>
<tr>
<td>Give morphine (1-5 mg iv), in case of allergy give meperidine.</td>
<td></td>
</tr>
<tr>
<td><strong>Initial management of acute ischemic pain in MI:</strong></td>
<td>The university cardiologists stated prescribing iv beta-blockers and nitrates routinely in all acute MI patients, unless contraindicated.</td>
</tr>
<tr>
<td>If opioids fail to relieve pain on repeated administration → Give iv beta-blockers or iv nitrates.</td>
<td></td>
</tr>
<tr>
<td><strong>Management of ventricular tachycardia post MI:</strong></td>
<td>The university cardiologists stated using amiodarone instead of lidocaine.</td>
</tr>
<tr>
<td>If high risk of recurrent VF → Give iv lidocaine</td>
<td></td>
</tr>
</tbody>
</table>

q.q.h.: every four hours.

In addition to the above categories of feedback, elaboration on the study setting-specific issues occurred in all the rounds. These were not included in the templates. However, they are described below, because they give further insight into the study setting.

4.3 The Jordanian Setting-specific Issues:

Elaboration on the study settings’ issues were mainly given by the MOH cardiologist in the form of written comments. The university and private cardiologists commented only
on the availability of some drugs in their hospitals. The issues included:

**Drug Policy and Procurement:**
The MOH cardiologist described the current regulations for drug procurement at the MOH sector as old and needed overhauling. The cardiologists stated that decisions on drug procurement do not take into consideration evidence-based practice (i.e. findings from clinical trials and guidelines). Alternatively, personal experience and drug costs were reported to be the major determinants, and locally manufactured drugs were given preference. The cardiologist added that the committees appointed to approve drug purchases are - in most cases- formed of non-practising physicians. Physicians were perceived as better candidates to decide on drug procurement, because of their clinical experience and up-to-date knowledge on drugs.

**Prescribing Habits and Practice:**
The MOH cardiologist stated that practice at his hospital was based on physicians’ experience. Whereas, management protocols were lacking in most hospitals even in other sectors. Nevertheless, the cardiologist stated growing awareness among practitioners on the need for treatment protocols.

In response to the reviewed DUE templates, the cardiologist commented on some local practices at the MOH hospital. These included under-utilisation of beta-blockers in heart failure, and over-prescribing of nitrates post myocardial infarction in the absence of angina. This latter was attributed to the misunderstanding by most doctors of the indications for use of nitrates.

**Patient Education and Drug Compliance:**
The MOH cardiologists reported that patient education on the management of their diseases and life-style modification was poor. Patient adherence to therapy was also believed to be problematic. An example was given on patients’ non-adherence to diuretic therapy after the resolution of fluid retention. The cardiologist stated that many factors contributed to patient non-compliance, yet specified inadequate patient education as its major cause.
Drug Availability:
Throughout the assessment of the templates, the cardiologists, except the one from the private hospital, made comments on the drugs unavailable in their settings. Table (26) shows the reported unavailable drugs in the three hospitals at the time of the study. Drug unavailability is clearly a more serious issue at the MOH hospital. Whereas more drugs were available at the university and the private hospitals. When asked, the private cardiologist stated that only a few members of the beta-blockers group were unavailable at the hospital, because they were not in the market. Drug shortages at the MOH hospital were ascribed to the current procurement policies. They were reported to hinder adherence to the guideline criteria on drug use, e.g. use of clopidogrel and ticlopidine in patients with acute coronary syndrome. Similarly, the guideline recommendation on not to switch between the different drug preparations (e.g. nicotinic acid) was perceived as inapplicable at the MOH setting, because what was available at the hospital determined what was prescribed.

Table (26): Drugs Unavailable in the Study Hospitals at the Time of Study:

<table>
<thead>
<tr>
<th>University</th>
<th>MOH</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bepridil, hydralazine, cilazapril (not commonly used in Jordan), milrinone (not used in Jordan).</td>
<td>Bepridil, nicorandil, clopidogrel, ticlopidine, abciximab, tirofiban, eptifibatide, enoxaparin, hirudin, tenecteplase, ramipril, torasemide, GTN (spray, ointment, buccal, oral-sustained release), isosorbide mononitrate, milrinone, metolazone, some beta-blockers.</td>
<td>Few members of the beta-blockers group, which were not available in the market.</td>
</tr>
</tbody>
</table>

4.4 Final Version of the Templates:
Four templates were produced in the form of guidelines for the management of stable angina, unstable angina, myocardial infarction and heart failure (appendix, 10). These were locally adapted to the Jordanian settings (MOH, university and private hospitals).
The templates were comprehensive; detailing criteria on the prescribing and monitoring of CV medication, as well as the following up of CHD, HF and concomitant CHD/HF patients. They comprised:

1- The guideline-derived DUE criteria agreed by all the cardiologists.
2- The DUE criteria added by the cardiologists.
3- The amended guideline criteria based on "Jordanian practice".
4- The "Gold Standard" (disapproved guideline criteria for which no consensus was established).
Discussion:

*The Choice of the Guidelines:*

As discussed earlier in chapter three, the referral to established guidelines is a commonly used method to assess drug utilisation (Beaulieu et al, 2004; Silagy et al, 2002; Reid et al, 2001; Wu et al, 1998; Lindley et al, 1992). In this study, the ACC/AHA and ESC guidelines were chosen to develop the templates, because they are developed by a large number of cardiology experts through critical review of a wide evidence-based literature and experts consensus. Basing the templates on these guidelines would enhance their content validity and eliminate concerns on the appropriateness of the DUE criteria. Furthermore, the referral to guidelines would eliminate the possibility of unsystematic literature reviews (Hicks, 1994), which would undermine the validity of the criteria.

The ACC/AHA and ESC guidelines were well-known to the study cardiologists and strongly approved by them. This could endorse what has been reported in the interviews-in chapter two- that physicians are mainly influenced by the American and the British medical practice.

Despite the above advantages of using the guidelines limitations were encountered during the development of the templates. This was due to the unavailability of all relevant data in the guidelines. For instance, the ACC/AHA, and ESC guidelines recommended the management of dyslipidemia in CHD patients, stated therapy goals and benefits of treatment, without stating the dosing regimens, side effects or contraindications to lipid-lowering drugs. Therefore, the NCEP recommendations for using these drugs were consulted. It is advisable to use more than one source of data for the comprehensiveness of drug use criteria. While the literature showed that different beta-blockers have distinct impact on the outcome of myocardial infarction, based on their pharmacological properties (Freemantle et al, 1999). The ESC guidelines did not differentiate between the different beta-blockers.

*The Panel Cardiologists:*

Realising the strong ownership by physicians of practice in Jordan made it crucial to get
their support and have them involved in the development of the templates. The project has given indications on the willingness by the cardiologists to develop local practice guidelines. As explained in chapter three, experts in the field must be consulted when developing DUE criteria, otherwise the findings from DUE will be undermined (Jones and Hunter, 1995; Hunter et al, 1994; Hicks, 1994). Using opinion leaders was one of the strategies reported to change clinical practice (Wallace et al, 2001). This explains the choice of senior cardiology consults, who were opinion leaders to form the panel. It was expected to enhance the credibility of the templates, and consequently the findings from their application to a large group of practitioners.

Interestingly, the study cardiologists’ opinions, reflected in their feedback, on appropriate practice did not always match their actual practice. For instance, they stated using spironolactone in mild to moderate heart failure cases, despite agreeing with the guidelines on reserving it for severe cases. In other cases, the reason given by the cardiologists indicated unawareness of practitioners of the drug characteristics. For example, the reported use of pethidine rather than morphine in the management of ischemic pain in myocardial infarction at the MOH hospital, was justified by the wish to avoid risk of respiratory depression. Upon consulting available evidence, pethidine was stated as not the drug of choice in myocardial infarction (Van de Werf et al, 2003). Furthermore, it could cause respiratory depression at an overdose (BNF, 2002; BNF, 2004).

The Development of the Templates:
The method of developing the templates is similar to the Rand technique, yet with some modification. This entailed omitting the construction of the questionnaires used for panellists’ rating. The questionnaires would be inconveniently lengthy, if they were to include the criteria for CV drugs use and the follow up of patients in the four diseases investigated. Similarly, postal surveys were not used, as they have been reported as less suitable for long questionnaires (Bowling, 2002). In addition to the previously stated concerns on the reliability of the postal system in Jordan. Another modification to the Rand technique was to the way in which panellists made their assessment of the criteria.
It was kept explicit rather than implicit, through seeking the cardiologists’ rationale when assessing the criteria. This was to overcome the drawback of the Rand method in not making the factors considered by panellists explicit, which hinders the judgement on the suitability of the templates in other settings (Bowling, 2002).

Attention was paid to limit the number of rounds for developing the templates to three. This was to overcome inconvenience on the side of panellists, which was reported to occur with higher numbers of rounds (Fink et al, 1984).

Tailoring the templates to the different study hospitals was crucial, given the considerable differences between the public and the private hospitals as illustrated in the interviews in chapter two.

_The Jordanian Setting-specific Issues:_

The issues related to the study hospitals although discussed in depth in the second chapter, they were presented here due to their close relevance to drug utilisation. Interestingly, the issues raised by the cardiologists on drug availability, prescribing practice and patient education were very similar to those reported in the interviews conducted two years earlier. They further corroborated the reports calling for reforming the drug procurement processes at the MOH sector and having them based on informed decisions. The fact that drug purchase decisions are made by non-practitioners, and based on drug costs and personal experience, rather than scientific evidence raises doubts on the soundness of these decisions. The decision-making on drug purchase should involve practitioners and take into consideration evidence-based practice, as much as possible within the setting constraints.

Although it is realised that the drug availability at the three hospitals is continuously changing over time, the drugs reported unavailable at the time of the study were shown in the results section for two reasons. First, to further illustrate the extent of variation in the availability of drug and resources across the three study settings. Second, it will explain why the guideline criteria pertinent to the use of these drugs could not be applied by prescribers, when the assessment of Jordanian practice at the three hospitals is undertaken, as presented in the next chapter. The low drug availability at the MOH hospital is foreseen to hinder complying to the templates. This stem from the fact that
the MOH cardiologist agreed with the drug use criteria on giving clopidogrel in unstable angina, yet could not adhere to it due to the unavailability of the drug. The same applies to heparin infusion method, despite approving the guideline-recommended weight-adjusted mode, it can not be implemented due to inadequate laboratory services and patient monitoring.

Poor patient education reported in this chapter further stresses the need for patient counselling services. Albeit physicians believe in the importance of these services to improve patient adherence to therapy. They are still lacking in all hospitals. Strategies for the effective introduction of these services must be devised.

Prescribing Habits and Clinical Practice Guidelines:
None of the study hospitals have practice guidelines or formularies. Guidelines are expected to standardise practice, improve the quality of care, rationalise resources and reduce costs. A lot of effort, time and money is devoted by health authorities in international settings to produce guidelines. Furthermore, in many settings the implementation of guidelines is becoming mandatory, e.g. the NICE guidelines. These measures are stimulated by the large variation in practice and the presumption that some of it is inappropriate. Other drives are the overuse of resources, especially with the growing pressures for cost containment and waste reduction, due to the rising health care costs and demand (Costantini et al, 2001; Woolf et al, 1999). Also, the underuse of medication, which is evident in many DUE studies, and is believed to compromise the quality of care (Pearson et al, 2001; Luzier et al, 1998; Bart et al, 1997). All of these pressures are applicable to the Jordanian setting, and endorse the initiative for having guidelines developed and implemented locally.

Guidelines would enhance practice through reassuring practitioners on the appropriate treatment to use, and drawing their attention to ineffective and wasteful practices. A systematic review of the evaluation of guidelines’ effectiveness concluded significant improvements in the process and outcome of care following the introduction of guidelines (Grimshaw and Russell, 1993). Reid et al (2001) found significant improvements in the prescribing of CV medication post myocardial infarction with the
dissemination of local guidelines. Similarly, Iliadis et al (1999) found greater use on admission and earlier administration of anti-ischemic drugs in unstable angina patients with the dissemination of guidelines, which resulted in better patient outcome.

Guidelines also support quality assurance processes through providing quality standards, e.g. audits (Woolf et al, 1999). Furthermore, their cost-effectiveness was established with the several reports on significant reduction in costs of care with the implementation of guidelines (Shibata et al, 2005; Debrix et al, 1999; Guterman and VanRooyan, 1998).

Nonetheless, evidence on the lack of effectiveness of guidelines to influence practice and therapy outcome also exists (Beaulieu et al, 2004; Weingarten et al, 1994). Benefits from guidelines are conditional to the level of adherence to them. It is crucial to assure successful introduction, dissemination and implementation of the guidelines (Grimshaw and Russell, 1993). The clinical context and relevance of guidelines are important determinants of adherence (Grimshaw and Russell, 1993), as well as user-friendliness and availability (Beaulieu et al, 2004; Costantini et al, 2001; Cranney et al, 2001; Weingarten; 2000). Furthermore, involving physicians in the drafting and implementation of the guidelines was associated with greater adherence (Thilly et al, 2003; Guterman and VanRooyan, 1998; Putnam and Curry, 1985). This latter measure is crucial in a setting like that in Jordan, given the strong ownership of practice and dominance by physicians. Other measures to smooth the successful introduction of guidelines include combining them with other strategies such as continuing medical education (Beaulieu et al, 2004), patient-specific decision support (Debrix et al, 1999), active care management groups (clinical groups to focus on a particular issue) (Costantini et al, 2001; Wallace et al, 2001), and clinical pathways (Ferry et al, 2004; Cheah, 2000).

Despite the above evidence on the benefits of guidelines, one should not be oblivious to their limitations. The fact that guidelines may be insensitive to individual patients’ needs has been reported in the literature (Cranney et al, 2001), as well as by Jordanian practitioners in the interviews (chapter 2). This has been perceived as one of the barriers to adherence to guidelines. It is important to emphasise that guidelines are tools to assist
and not to substitute practitioners’ judgement (Costantini et al, 2001).

Limitations:
Of the limitations of the method used in this study is the small panel size. However, this has been compensated for by having senior cardiologists, who are opinion leaders in their hospitals, which is expected to increase the validity and credibility of the templates to other practitioners. The method used in developing the templates is believed to be the most pragmatic approach, especially that the concept of developing guidelines for the assessment of local practice is not embedded in the Jordanian health care system. Besides, national treatment protocols do not exist. This stage of the project tested the concept and methodology of establishing practice assessment tool and local treatment guidelines, which proved to be achievable in the Jordanian setting. The next step will be to test this tool and use it to assess actual practice.

Implications of This Chapter:
Having developed the templates and tailored them to the Jordanian settings, the next chapter will involve their application to evaluate the use of CV drugs in CHD and HF patients at the three study hospitals. This will give insight into the appropriateness of Jordanian clinical practice and allow the identification of gaps in the drug utilisation processes.
Chapter Six:  
Evaluation of Cardiovascular (CV) Drug Use in Coronary Heart Diseases (CHD) and Heart Failure (HF).

Introduction:  
Following on from the previous chapter, this chapter presents the application of the developed templates of DUE criteria to evaluate the use of CV medication in coronary heart diseases (stable angina, unstable angina, and myocardial infraction), heart failure (HF), and concomitant CHD and HF patients at the three study hospitals.

Aim:  
First, to evaluate CV drug prescribing, monitoring and follow up of coronary heart disease and heart failure patients at the three study hospitals. Second, to provide indications on gaps in CV drug use and to propose recommendations to optimise it, highlighting the role of pharmacists in cardiac patients care.

Objectives:  
1- To evaluate the ongoing CV drug use practices at the three study hospitals against the developed templates of DUE criteria. This involves the assessment of CV drug prescribing (choice of drugs, doses, frequency, route of administration), therapy monitoring and follow up of patients (clinical investigations and laboratory tests) for stable angina, unstable angina, myocardial infarction, heart failure and concomitant CHD/HF patients.

2- To assure reliability of the application of the templates to evaluate drug use processes.

3- To validate the results from the evaluation of CV drug use by submitting a random sample of cases for validation by the study cardiologists.
4- To identify gaps in CV drug use in CHD and/or HF patients in the light of the developed templates, and to propose recommendations to optimise practice, highlighting the role of pharmacists in secondary care for CHD and HF patients.

Methodology:

1. Sampling and Recruitment:
The cardiac patients screened at the three study hospitals, as illustrated in chapter four, who were diagnosed with stable angina (SA), unstable angina (UA), myocardial infarction (MI), heart failure (HF) whether with or without arrhythmia, and concomitant heart failure and coronary heart diseases were included for the evaluation of CV drug use practices at the three study hospitals (MOH, private, university). These included 61 patients, distributed as: 9 SA, 16 UA, 10 MI, 10 HF, 10 SA/HF, and 6 UA/HF patients. Patient data were coded, their identity, type of hospital and the treating physician were anonymised.

2. Instruments and Procedures:

2.1 Preparation of Case Vignettes and Checklists:
Case vignettes (appendix, 12a) were prepared for the 61 CHD and HF patients. Each case vignette summarised the patient demography, weight, present health complaint, medical and drug history, findings of physical examination, diagnosis, physician’s orders, medication prescribed on the day of contacting the patient, and during the follow up of patient (until the patient discharge or the end of the 5-day study period, whichever occurred earlier). Additionally, the results of laboratory tests and patient follow up notes were also included.

Since the templates (appendix, 10) were in a guideline format, checklists were designed (appendix, 12b) to enable the application of the templates to the patients’ data to facilitate the process of evaluation of drug use. Six checklists of explicit DUE criteria were developed based on the templates, one checklist for each of the cardiac diseases investigated: SA, UA, MI, HF, SA/HF and UA/HF. The checklists were organised into
four sections: 1- Drug prescribing (choice of drugs, duration, contraindications).
2- Dosing (dose, route of administration, frequency, rate of infusion).
3- Therapy monitoring (ischemic pain, blood pressure, heart rate, weight, edema, laboratory tests, their frequency).
4- Follow up of patients (patient response to therapy).

The checklists were field tested by applying them to a sample of cases to assure their effectiveness in the evaluation of therapy, and amended accordingly. Then were also approved by the three study cardiologists.

3. Data Processing and Analysis:

3.1 Assessment of CV Drug Prescribing, Monitoring and Follow Up of Patients and Identification of Gaps in Practice:

The Jordanian practice of CV drug use was evaluated against the DUE criteria listed in the checklists for each of the 6 disease subgroups. The use of CV drugs was assessed throughout the period of contact with the patients (minimum 1 day and maximum 5-day period). The assessment of appropriateness of CV drug use involved the prescribing and non-prescribing of the medication. It covered the choice of drugs, dosing, frequency, route of administration, duration, and contraindications. Delays in therapy were also assessed. They involved situations where drugs were not administered on the first day of hospitalisation although there were no contraindications. The CV drug classes assessed were: anti-platelets, beta-blockers, ACE-Inhibitors, angiotensin receptor blockers (ARBs), nitrates, calcium channel blockers (CCB), diuretics, digoxin, anticoagulants (oral and parenteral), fibrinolytics, opioid analgesics and adjunct anti-emetics, lipid-lowering drugs, and the combination of hydralazine and nitrates (in HF patients). The assessment excluded the use of anti-arrhythmic drugs, because the study cardiologists agreed on leaving the management of arrhythmia to the physician’s discretion, due to the individuality of patient cases. Similarly, the use of antiplatelets (except aspirin) and anticoagulants in SA patients undergoing cardiac procedures, and in CHD patients post coronary bypass surgery (CABG) was also excluded because it was beyond the scope of the templates. The assessment of myocardial infarction (MI) therapy was divided into an
acute and a post-acute phase. The acute phase was agreed on with the cardiologists as the first 24 hours of hospitalisation, given that the onset of MI symptoms was on the same day of admission.

The assessment of CV drug monitoring involved the laboratory investigations done during contacting the patient. However, in some cases when patients were contacted during their hospitalisation, and not on admission, the laboratory investigations done before contacting the patient (out of the study period) were included for the more accurate evaluation of therapy. For example, lipid profile done before contacting the patient were included in the assessment of monitoring of anti-lipids, because the templates recommended obtaining the lipid profile before the inception of therapy. The assessment covered the monitoring of ischemic pain, blood pressure, heart rate, renal function, edema, weight, electrolytes, lipid profile, liver function tests, haematology indices (PTT, INR, platelets, white blood cells, haemoglobin). Follow up of patients was evaluated for patients who were contacted for more than one day. This involved the assessment of follow up on patient vital signs, disease signs and symptoms, therapy side effects (e.g. blood pressure, heart rate, ischemic pain, edema, shortness of breath, bleeding signs with anticoagulants, signs of digoxin toxicity).

Gaps in drug utilisation processes (prescribing, monitoring and follow up of patients) were highlighted for the whole sample.

3.2 Assurance of Inter-rater Reliability:

Reliability of the application of the templates to case-vignettes was assured by the submission of randomly selected SA, UA/NSTEMI, MI and HF cases to external assessors. This involved 21% of the cases. Random selection of the cases entailed giving each of the 61 cases a number, then a “draw-from-the-pot” took place. The assessors were one of the project supervisors and two peer pharmacists. All assessors had experience in the area of cardiovascular drug use. They were provided with copies of the checklists, the templates and the case-vignettes, and were asked to assess actual practice against the templates using the checklists. This step, in addition to assuring the reliability of the templates as a tool for therapy assessment, aimed at verifying the assessment of practice by experienced pharmacists before the submission of cases to
cardiologists for evaluation. Feedback of both the researcher and the assessors was compared and unified in the light of the templates. Practice assessment deviating from the templates were accordingly amended.

3.3 Validation of the Assessment of Drug Utilisation:
The assessment of practice was validated through the submission of a stratified random sample of cases (SA, UA, MI, HF, SA/HF, and UA/HF) for review by the three study cardiologists, from the university, MOH and private hospitals. Random case selection was conducted as mentioned above. Twenty two cases (almost 40% of cases) were validated. The cardiologists’ feedback was compared to each other and analysed relative to the templates. If the cardiologists unanimously agreed with the assessment, in harmony with the templates, then the assessment was considered valid. Discordant cardiologists’ feedback was handled as follows: a) if the majority agreed with the assessment and complied to the templates, the assessment was considered valid, b) if the majority disagreed with the assessment, and deviated from the templates, the assessment was still considered valid.
The assessment was amended if: a) it erroneously deviated from the templates (slip by the researcher), and was corrected by any of the cardiologists.
b) the cardiologists unanimously disagreed with the assessment and the templates. The amendments were described along with the cardiologists’ justification of deviation from the templates, whenever available.

The SPSS 10.00 software was used for data analysis. Data were coded, entered into the software and double checked for accuracy. Descriptive statistics involved the use of frequencies and percentages to present the frequency of prescribing CV drugs.
Results:

1. Feedback on the Reliability of the Templates:
The reliability of the templates as a tool for the assessment of therapy was high (over 95%). The assessment by the researcher and the external assessors agreed in all the cases except four, which were amended accordingly (e.g. a lapse by the researcher rectified to comply with the templates). Additionally, one of the assessors suggested leaving the assessment of antiarrhythmic use in MI patients to the discretion of cardiologists, because it was not covered thoroughly in the templates.

2. Feedback on the Validation of the Assessment of CV Drug Use:
The cardiologists agreed with the majority of the researcher’s assessment of practice. In few instances, the feedback by one or two of the cardiologists deviated from the templates. Examples were:
1- Simvastatin dose was recommended as 20- 80 mg. If combined with fibrates, nicotinic acid or ciclosporin a 10 mg dose was acceptable. However, one of the cardiologist considered simvastatin 10 mg appropriate, stating that it was usually effective and commonly used for cost purposes.
2- Perindopril was not among the popularly used ACE-Inhibitors in CHD. None of the guidelines, the BNF or the consensus panel stated a dose for the drug in UA. Only one cardiologist suggested using the same dose approved for hypertension and HF.
3- One of the cardiologists supported giving nitrates post MI to all patients even in the absence of angina, which was not recommended by the templates.
4- Two of the cardiologists stated that the use of nitrates alone in HF is a common practice in Jordan, whereas hydralazine was never used. This deviated from the templates, where the use of either nitrates or hydralazine alone in HF was not recommended.

Amendments:
Eight amendments were made to the evaluation of practice, when the cardiologists’ feedback unanimously deviated from the templates. These were:
1- Not prescribing beta-blockers to one SA patient, which was considered appropriate, despite deviating from the templates, because the patient was clinically unstable.
Chapter Six

Delaying beta-blockers was suggested until the patient condition was stabilised.

2 - Beta-blockers prescribed in one UA patient with a history of bronchial asthma, was considered appropriate by the cardiologists upon reviewing drug history and physical examination notes of the patient.

3- Cardiologists disagreed with the assessment of anti-arrhythmics use in one MI patient. It was suggested to exclude antiarrhythmic use from the assessment. The cardiologists agreed it should be left to physicians’ discretion, besides it required risk stratification, which was not discussed in the templates.

4- All the cardiologists agreed on using higher doses of furosemide injections, exceeding the template-recommended 20-50 mg iv dose. Doses of 80-120 mg up to three times a day were suggested.

5- Although the templates stated diabetes mellitus was not a contraindication to beta-blockers, not prescribing beta-blockers in one SA/HF patient whose blood sugar levels were very high, was considered appropriate by the cardiologists. Delaying the dose of beta-blockers was suggested until the blood sugar levels were controlled.

6- The prescribing of telmisartan, an ARBs, alternative to ACE-Inhibitors in 1 SA/HF patient was considered appropriate by the cardiologists, despite no evidence of previous use or intolerance to ACE-Inhibitors.

7- Prescribing of beta-blockers via oral route in the early management of 1 UA/HF patient - not intravenously as recommended by the templates- was considered appropriate by the cardiologists.

8- The prescribing of spironolactone in one UA/HF patient was considered appropriate by the cardiologists, although there was no indication for spironolactone as per the templates.

3. Findings From the Assessment of CV Drug Use and the Gaps in Practice:

The results from the evaluation of CV drug use are presented for 59 out of 61 patients. Data were missing for 2 patients. First, the results from the assessment of CV drug prescribing are presented across all conditions to give an overall idea on the appropriateness of practice. Subsequently, the results from the assessment of CV drug prescribing, monitoring and follow up of patients are presented for each of the six cardiac disease groups namely: stable angina, unstable angina, myocardial infarction, heart failure, concomitant stable angina/heart failure and unstable angina/heart failure.

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3.1 Appropriateness of CV Drug Use Across All Disease Groups:
The results from the assessment of drug use (table, 27) involve the prescribing and non-prescribing of medication (i.e. the drug appropriately prescribed or omitted vs. the drug inappropriately prescribed or omitted). Among all CV drugs, loop diuretics, CCB, aspirin and LMWH were of most appropriately used. Conversely, drug use was least appropriate for lipid lowering drugs. Reasons for not being able to assess the use of some drugs in a proportion of the sample are explained in section 3.2.

Table (27): Appropriateness of CV Drug Utilisation Practice:

<table>
<thead>
<tr>
<th>Drug</th>
<th>No. of Patients (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Appropriate (%)</td>
<td></td>
</tr>
<tr>
<td>Antiplatelets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>53 (91.4)</td>
<td>58 (100)</td>
</tr>
<tr>
<td>Ticlopidine/</td>
<td>17 (58.6)</td>
<td>29 (100)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>46 (67.6)</td>
<td>68 (100)</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>41 (60.3)</td>
<td>68 (100)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>46 (67.7)</td>
<td>68 (100)</td>
</tr>
<tr>
<td>CCB</td>
<td>63 (92.6)</td>
<td>68 (100)</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>8 (16.7)</td>
<td>48 (100)</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>24 (92.3)</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>18 (69.2)</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>25 (64.1)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>LMWH</td>
<td>19 (82.6)</td>
<td>23 (100)</td>
</tr>
<tr>
<td>Fibrinolytics</td>
<td>6 (60.0)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Opioids*</td>
<td>26 (86.7)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>23 (88.5)</td>
<td>26 (100)</td>
</tr>
</tbody>
</table>

* Not a CV drug, however, stated here for its use in the management of ischemic pain in MI.
3.2 Appropriateness of CV Drug Use Classified by the Cardiac Disease Group:

3.2.1 Stable Angina:

3.2.1.1 Prescribing of Drugs:

The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (14). Sixty eight percent (68%) of CV drug use was appropriate (50% appropriately prescribed and 18% appropriately not prescribed), 20% was inappropriate where the drugs were not prescribed as recommended despite no contraindication (CI), and 11% of drug use could not be assessed.

![Figure (14): Assessment of CV Drug Use in SA.](image)

The details of the evaluation of each of the CV drug groups are as follows:

- The prescribing of aspirin was appropriate in 8 out of the 9 SA patients (figure, 14), however, it was inappropriately delayed in 1 patient. Aspirin was not prescribed in 1 patient due to allergy, alternatively, clopidogrel was prescribed as recommended.

*Appropriate CV drug use/total CV drug use.*
• The use of beta-blockers was appropriate in 6 out of 9 patients (figure, 14). However, therapy was inappropriately delayed in 1 out of the 6 patients. Beta-blockers were not used in 3 out of the 9, despite having no contraindication.

• ACE-Inhibitors were appropriately used in only 2 out of the 9 patients (figure, 14). However, in 1 of the 2 patients, cilazapril, was used which was not among the agents of choice. ACE-Inhibitors were not prescribed as recommended in 7 out of the 9 patients despite having no CI. In 1 out of the 7 patient, ARBs were prescribed although there was no proof of intolerance to ACE-Inhibitors.

• Nitrates and CCB were appropriately used in all the 9 patients (figure, 14). The use of nitrates was inappropriately delayed in 2 patients.

• The use of lipid lowering drugs could not be assessed in 6 out of the 9 patients (figure, 14), because data on lipid profile were unavailable or incomplete. The use of antilipids was appropriate in 2 out of the 9 patients, who had elevated cholesterol levels. However, the choice of agents was not optimal, i.e. fibrates were used in lowering LDL, where statins were more preferable, and statins were used to manage elevated TG, where fibrates were more preferable. The drugs were inappropriately not prescribed in 1 patient eligible to statins.

3.2.1.2 Drug Dosing:
Dosing of CV drugs was appropriate in 68% of dosing orders (table, 28). Under-dosing mainly occurred with beta-blockers. Dosing could not be assessed mainly for intravenous nitrate doses because the rate and mode of infusion (in 3 dosing orders) and the infusion duration (in 1 dosing order) were not documented. Moreover, the dosing of oral ISDN in one case could not be assessed due to lack of documentation of the dose. Similarly, 1 out of 8 aspirin dosing orders could not be assessed due to the lack of documentation of dose or brand.
### Table (28): Appropriateness of CV Drug Dosing in SA Patients:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total</th>
<th>Appropriate</th>
<th>Below</th>
<th>Above</th>
<th>Could not assess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>8</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nitrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTN</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>ISDN</td>
<td>9</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>CCB</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Trimetazidine</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (%)</td>
<td>34 (100)</td>
<td>23 (68)</td>
<td>5 (15)</td>
<td>0</td>
<td>6 (17)</td>
</tr>
</tbody>
</table>

#### 3.2.1.3 Therapy Monitoring and Follow Up of Patients:

- **Ischemic pain**: Only in 2 out of 9 patients that daily monitoring and follow up of ischemic pain, blood pressure (BP) and heart rate were done. Monitoring of ischemic pain was incomplete in the remaining 7 patients (either nothing documented, only on admission, or during hospitalisation and not on admission). Data on monitoring and follow up of BP and heart rate were missing for 1 patient and incomplete in 6 out of 9 patients (either only on admission, nothing documented, or inadequately monitored during hospitalisation).

- **Renal function**: It was monitored in 6 out of 9 patients, not monitored in 1 patient and incomplete in 2 patients (only urea levels were measured and not creatinine).

- **Lipid profile**: only in 2 out of 9 patients that a lipid profile was done. It was incomplete in 1 patient, where LDL was not measured, and not done in 6 patients. Liver transaminases were monitored in only 1 out of the 3 patients prescribed statins.
3.2.2 Unstable Angina/Non-ST-segment Elevation Myocardial Infarction:
Practice was assessed in 14 out of the 16 UA patients. This is because data were missing for 1 patient, and the second patient was a case of UA and LAD actasia, whose management was still controversial and beyond the scope of the template, hence the patient was excluded, upon the cardiologists’ recommendation.

3.2.2.1 Prescribing of Drugs:
The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (15). Sixty three percent (63%) of CV drug use was appropriate (38% appropriately prescribed and 25% appropriately not prescribed). Conversely, 24% of drug use was inappropriate; in 4% the drug should not have been prescribed, whereas in 20% the drug was not prescribed as recommended despite no CI. Drug use could not be assessed in 12% of practice (i.e. drug use which could not be assessed/total drug use).

![Figure (15): Assessment of CV Drug Use in UA/NSTEMI.](image-url)
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The details of the evaluation of each of the CV drug groups are as follows:

- Nitrates were appropriately prescribed in 12 out of the 14 patients (figure, 15); ISDN in 10 patients, GTN in 1 patients, and both drugs concomitantly in 1 patient. Therapy was inappropriately delayed in 1 patient. Not prescribing nitrates was inappropriate in 1 patient who had no CI, and it could not be assessed in another patient due to inadequate documentation of BP levels.

- Beta-blockers were appropriately prescribed in 10 out of the 14 patients, and not prescribed in 1 patient who was clinically unstable (underwent CABG and was receiving a positive inotropic agent). Therapy was inappropriately delayed in 2 out of 10 patients. Two out of 14 patients were not prescribed the drug as recommended, despite having no CI. Practice could not be assessed in 1 out of 14 patient due to inadequate documentation of BP levels.

- ACE-Inhibitors were prescribed in 5 patients (figure, 15), which was appropriate in 4 patients and could not be assessed in 1 patient due to inadequate documentation of BP levels. The choice of agent was suboptimal in 2 out of the 5 patients, where perindopril and fosinopril were prescribed, which were not among the ACE-Inhibitors of choice in CHD. On the other hand, ACE-Inhibitors were inappropriately not used in 9 out of 14 patients who had no CI.

- CCB: diltiazem was prescribed in 5 out of 14 patients (figure, 15), which was appropriate in 2 patients, inappropriate in 2 patients, and could not be assessed in 1 patient. In the latter patient CCB was added to therapy before assessing the patient response to beta-blockers and nitrates, as recommended. The choice of agent was suboptimal in 1 out of the 5 patients, where amlodipine should have been prescribed instead of diltiazem because the patient had bradycardia.

- Morphine was inappropriately not prescribed in 1 out of the 14 patients, who had a sustaining ischemic pain despite therapy. In another patient Morphine was prescribed on as-needed basis, without prescribing a concomitant anti-emetic, opposite to what was recommended.
• Antilipids: Out of 14 patients, the use of antilipids could not be assessed except in 2 patients. One patient was appropriately prescribed the medication, however, the choice of agent, whether statin or fibrate, could not be assessed, because of the incomplete lipid profile (LDL was not measured). The second patient was not prescribed the drug, despite having elevated cholesterol levels and no CI. Therapy could not be assessed in the remaining 12 patients, because a lipid profile was not done.

Antiplatelets and Anticoagulation Therapy:
• All 14 patients were prescribed aspirin as recommended, however, it was delayed in 1 patient.

• Heparin and LMWH were appropriately prescribed in 8 and 2 patients out of the 14 patients, respectively. Both drugs were inappropriately concomitantly prescribed in 1 out of the 14 patients. On the other hand, neither heparin nor LMWH were prescribed in 2 out of the 14 patients despite no CI, which was inappropriate. One patient could not be assessed due to undergoing CABG on admission day, which was beyond the scope of the templates. Out of the 8 patients appropriately prescribed heparin, the duration of therapy (recommended: 2-5 days) was appropriate in 5 patients, inappropriate in 1 patient, and could not be assessed in 2 patients due to inadequate documentation.

• While ticlopidine was appropriately prescribed in 4 out of 14 patients, none of the patients was prescribed clopidogrel. The drugs were appropriately skipped in 2 patients who were planned to undergo CABG. Conversely, neither of the drugs were prescribed in 8 out of the 14 patients despite having no CI.

• GP IIb/IIIa Inhibitors were appropriately prescribed in 1 out of the 14 patients, who was undergoing PCI. The drugs were appropriately not prescribed in 7 patients (6 patients not undergoing PCI and 1 patient undergoing CABG). Conversely, the drugs were inappropriately not prescribed in 5 patients, despite undergoing PCI and having no CI. Practice could not be assessed in 1 out of the 14 patients, because the patient underwent CABG on admission, which was beyond the scope of the templates.
• Warfarin was prescribed in 2 out of the 14 patients, which could not be assessed in 1 of the patients because it was beyond the scope of the templates (post CABG), as for the second patient it was prescribed for non-cardiac indication.

3.2.2.2 Drug Dosing:
Dosing of CV drugs was appropriate in 60% of dosing orders (table, 29). Inappropriate dosing mainly involved intravenous heparin infusions, where 9 of the 13 prescribed

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total number</th>
<th>Appropriate</th>
<th>Below</th>
<th>Above</th>
<th>Could not assess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GP IIb/IIIa inhibitors</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Nitrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTN</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ISDN</td>
<td>11</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>CCB</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stat</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Infusion</td>
<td>13*</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>LMWH</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total (%)**</td>
<td>76 (100)</td>
<td>46 (60.5)</td>
<td>7 (9.5)</td>
<td>8 (10.5)</td>
<td>11 (14.5)</td>
</tr>
</tbody>
</table>

* Four out of the 13 heparin infusions were inappropriate, yet not assessed in terms of below or above the recommended dose, because the prescribed regimen was a fixed-dose intermittent iv injection, whereas the recommended regimen was weight-adjusted, hence, they could not be compared.

** Numbers do not add up to the total sum, because they do not include the 4 (5%) fixed-dose heparin infusion mentioned above.
infusions were inappropriate; 5 above the recommended dose, and 4 were prescribed as fixed-dose intermittent iv injections, which deviated from the recommended weight-adjusted regimen. Similarly, the dosing practice could not be assessed predominantly for intravenous medication, because either the infusion rate or duration were not documented (e.g. GTN, ISDN, heparin, tirofiban), the patient weight was not documented (e.g. tirofiban, enoxaparin, and heparin, whose recommended doses are weight-adjusted), or there was no consensus or guideline dose to compare with (e.g. ACE-Inhibitors; fosinopril and perindopril, not agents of choice in CHD, hence no standard dose existed).

The route of administration of nitrates was appropriate in 12 dosing orders, and inappropriate in one, where it should have been prescribed intravenously rather than orally, because the patient had continuing ischemic pain, which was not relieved by oral therapy. For the same reason, 2 out of the 10 beta-blocker dosing regimens should have been initiated as intravenous rather than oral therapy.

3.2.2.3 Therapy Monitoring and Follow Up of Patients:

- Ischemic pain: while pain was monitored in 8 out of the 14 patients, nothing was documented in 6 patients. Follow up on pain was evaluated in 11 out of 14 patients. Only in 4 out of the 11 patients that pain was followed up, which was inadequate in 3 patients (not on daily basis). The remaining 7 patients had nothing documented on their response to anti-ischemic therapy in the follow up notes. BP and heart rate were monitored on admission in 11 out of 14 patients, and nothing was documented in 3 patients. Follow up of BP and heart rate was evaluated in 11 out of 14 patients. They were followed up in 4 and 5 patients only, respectively, which was incomplete except in 2 patients. Renal function (serum creatinine and urea) was monitored in 11 out of 14 patients. The remaining 3 patients either had urea only (in 1 patient) or no monitoring (in 2 patients) done.

- Lipid lowering therapy: Only 2 out of the 14 patients had a lipid profile done, which was incomplete in 1 patient, because LDL was not measured. Statin therapy was not
monitored in any of the 3 patients prescribed the drug (liver transaminases not done).

- Antiplatelets and anticoagulants: None of the patients prescribed heparin had aPTT monitored as recommended, despite having a documented physicians order in 4 patients. aPTT monitoring was inadequate in 2 patients, i.e. not measured on daily basis or upon dose change. On the other hand, aPTT was measured in 1 patient who was not prescribed heparin. Haemoglobin and platelet count were monitored once during heparin therapy in 4 patients. Two patients had haemoglobin only monitored, and none of the patients had hematocrit monitored during therapy as recommended.

Out of 4 patients prescribed ticlopidine, the platelets and WBC count were monitored in 2 patients. Only platelets were monitored in 1 patient and no monitoring took place in 1 patient. As for the 1 patient prescribed GP IIb/IIIa inhibitor, the haemoglobin and platelet count were not monitored as recommended.

3.2.3 Myocardial Infarction:

3.2.3.1 Prescribing of Drugs:

a) Acute Phase:

The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (16). Seventy nine percent (79%) of CV drug use was appropriate (49% appropriately prescribed and 30% appropriately not prescribed). Conversely, 20% of drug use was inappropriate; in 8% the drug should not have been prescribed, whereas in 12% the drug was not prescribed despite no CI. One percent of drug use practice could not be assessed.

The details of the evaluation of each of the CV drug groups are as follows:

- Antiplatelets and Anticoagulants: Aspirin and heparin were prescribed to all 10 patients as recommended.

- Opioids and anti-emetics: Opioids were prescribed in 4 out of 10 patients, which was appropriate in 2 patients, who were prescribed morphine, and inappropriate in 2 patients, who were prescribed pethidine, which was not recommended in MI. Only 1 of
the 4 patients was prescribed an antiemetic, adjunct to opioid therapy, as recommended (the second dose of anti-emetic, as shown in figure (16) was given for non-cardiac cause (nausea).

- Fibrinolytics were appropriately prescribed in 5 out of the 10 patients, and not prescribed in 1 patient who underwent primary PCI (figure, 16). Not prescribing fibrinolytics was inappropriate in 3 out of the 10 patients, who had no Cl. In one of the patients this resulted from missing the diagnosis for UA. Not using fibrinolytics could not be assessed in 1 patient, because the time to admission post the onset of symptoms could not be identified.

- Beta-blockers: Beta-blockers were appropriately prescribed in 7 out of 10 patients, and not prescribed in 1 patient (figure, 16), due to hypotension. Beta-blockers were inappropriately not prescribed in 3 out of 10 patients, in 2 of them therapy was delayed to the post acute phase, despite having no Cl for early initiation of therapy.
• ACE-Inhibitors: ACE-Inhibitors were appropriately prescribed in 6 out of 10 patients (figure, 16). However, the choice of drug was suboptimal in 1 out of the 6 patients, where fosinopril was prescribed, which was not among the drugs of choice in CHD. Therapy duplication occurred in the same patient, who was prescribed enalapril and fosinopril concomitantly. Not prescribing ACE-Inhibitors was appropriate in 1 out of 10 patients, due to hypotension, and inappropriate in 3 patients, who had no CI.

• Nitrates: Oral ISDN was prescribed in 4 out of 10 patients, iv GTN in 1 patient, and both drugs concomitantly in 2 patients. Prescribing nitrates was appropriate in 2 out of 7 patients, who had ongoing ischemic pain despite opioid therapy and inappropriate in the remaining 5 patients. Conversely, nitrate use was appropriately skipped in 3 patients (figure, 16).

• None of the patients was prescribed CCB in the absence of drug indication, as recommended (figure, 16).

b) Post-Acute Phase:
Nine out of 10 patients were assessed in the post acute phase, because 1 of the patients was screened for 1 day only. The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (17). Sixty nine percent (69%) of CV drug use was appropriate (33% appropriately prescribed and 36% appropriately not prescribed). Conversely, 16% of drug use was inappropriate; in 12% the drug should not have been prescribed, whereas in 4% the drug was not prescribed despite no CI. Practice could not be assessed in 15% of drug use.

The details of the evaluation of each of the CV drug group are as follows:
• Antiplatelets and Anticoagulants: Aspirin was prescribed as recommended in 8 out of 9 patients. Its use could not be assessed in 1 patient due to inadequate data. Out of the 9 patients only 2 had heparin therapy appropriately continued from the acute phase (figure, 17), and lasted for 48 hours, as recommended. The duration of heparin therapy exceeded the recommended period (24-48 hours) in 3 out of 9 patients. The use of
Figure (17): Assessment of CV Drug Use in Post Acute MI.

heparin could not be assessed in 4 out of the 9 patients, because therapy duration was unspecified. LMWH were appropriately prescribed in 1 out of the 9 patients, however, the drug chosen -tinzaparin- was not among the popularly used drugs. Ticlopidine was appropriately omitted in 8 patients as recommended, and used in 1 patient who underwent PTCA and stent.

• Beta-blockers: The use of beta-blockers was appropriate in all patients. The drug was not prescribed in 1 patient due to hypotension.

• ACE-Inhibitors: ACE-I were appropriately prescribed in 5 out of 9 patients, and not prescribed in 2 patients due to hypotension. Conversely, 2 out of 9 patients were not prescribed the drug, despite having no CI. The choice of agent was suboptimal in 1 patient prescribed fosinopril. Captopril and enalapril were prescribed in 1 and 3 patients, respectively.
• Nitrates: Prescribing nitrates was appropriate in 1 and inappropriate in 7 out of 9 patients. Only 1 out of the 9 patients was appropriately not prescribed nitrates, in the absence of angina.

• CCB: None of the patients was prescribed CCB, which was appropriate due to the absence of drug indication.

• Lipid Regulating Drugs: Of the 9 patients 2 were prescribed statins. This was appropriate in 1 patient who had elevated cholesterol levels. It could not be assessed in the second patient due to unavailability of a lipid profile. For the same reason, not prescribing the drugs in the remaining 7 patients could not be assessed.

3.2.3.2 Drug Dosing:
Dosing of CV drugs was appropriate in 66% of dosing orders (table, 30). Inappropriate dosing mainly involved intravenous heparin infusions and beta-blockers. Eight out of the 11 prescribed heparin regimens were prescribed as a fixed-dose intermittent iv injection rather than the recommended weight adjusted regimen. Dosing could not be assessed for 6% of the prescribed dosing orders. These included 2 ACE-Inhibitor and 1 LMWH dosing regimens (because fosinopril and tinzaparin were not among the drugs of choice in MI, hence, no guideline or consensus dose was available). Similarly, the dosing of oral nitrates (2 dosing regimens) in acute MI could not be assessed, because the drugs were not recommended orally in the early management of MI, as per the templates.

The route of administration was sub-optimal in 6 dosing regimens in the acute phase. These included 2 out of 5 fibrinolytic regimens, where alteplase was prescribed as a fixed-dose regimen rather than the recommended weight-adjusted regimen, 2 out of 7 beta-blocker dosing regimens, and 2 out of 3 nitrate regimens, which should have been prescribed intravenously rather than orally, because the patient was unresponsive to opioid therapy.
### Table (30): Appropriateness of CV Drug Dosing in MI Patients:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total Number of Dosing Orders in MI Patients (n= 10)</th>
<th>Total</th>
<th>Appropriate</th>
<th>Above</th>
<th>Below</th>
<th>Could not Assess</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiplatelets</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>18</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Anticoagulants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin stat</td>
<td>8</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Infusion</td>
<td>11*</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LMWH</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Anti-emetics</strong></td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Fibrinolytics</strong></td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Beta-blockers</strong></td>
<td>15</td>
<td>10</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>ACE-Inhibitors</strong></td>
<td>11</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Nitrates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTN</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ISDN</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Lipid Lowering</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>80 (100)</td>
<td>53 (66)</td>
<td>7 (9)</td>
<td>7 (9)</td>
<td>5 (6)</td>
<td></td>
</tr>
</tbody>
</table>

* Eight out of the 11 heparin infusions were inappropriate, yet not assessed in terms of below or above the recommended dose, because the prescribed regimen was a fixed-dose intermittent iv injection, whereas the recommended regimen was weight-adjusted, hence, they could not be compared.

** Opioids and adjunct anti-emetic therapy, despite not being classified as CV medication, they are stated here for their use in ischemic pain in CHD.

*** Numbers do not add up to the total sum, because they do not include the 8 (10%) fixed-dose heparin infusion mentioned above.

† In acute and post-acute MI patients.
3.2.3.3 Therapy Monitoring and Follow Up of Patients:

- Ischemic pain: Only in 3 out of 10 patients that ischemic pain was monitored on admission, and nothing was documented in 7 patients. Pain was followed up in 7 out of 9 patients, only in 1 patient that it occurred on daily basis. On admission monitoring of BP and heart rate was documented in 5 and 9 out of 10 patients, respectively. Follow up of BP and heart rate occurred in 9 and 7 out of 9 patients, respectively, however, it occurred on daily basis in 1 patient only.

Renal function (serum urea and creatinine levels) monitoring was done in 8 out of 10 patients, inadequate in 1 patient (only urea assessed) and not monitored in 1 patient.

- Anticoagulants: Out of the 10 patients prescribed heparin the PTT was measured in 3 patients only. None of the patients had PTT measured on daily basis as recommended during heparin therapy.

- Lipid Lowering Drugs: A lipid profile was obtained in 1 out of 10 patients only. However, it was incomplete, as HDL level was not assessed. No profile was obtained in 9 patients, although an order was documented in 2 patients. Liver transaminases were monitored in the 2 patients prescribed statins as recommended.

3.2.4 Heart Failure:

3.2.4.1 Prescribing of Drugs:

The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (18). Seventy two percent (72%) of CV drug use was appropriate (33% appropriately prescribed and 39% appropriately not prescribed). Conversely, 20% of drug use was inappropriate; in 9% the drug should not have been prescribed, whereas in 11% the drug was not prescribed despite no CI. Practice could not be assessed in 7% of drug use.
The details of the evaluation of each of the CV drug groups are as follows:

- **Diuretics and Potassium Supplements**: All 10 patients were appropriately prescribed a loop diuretic (figure, 18). Only in 2 out of the 10 patients that diuretic therapy was appropriately continued even after the resolution of fluid retention. This could not be assessed in 5 patients, because data on the status of edema were missing or incomplete. Spironolactone, was appropriately prescribed in 2 out of 10 patients, and not prescribed in 6 patients. Not prescribing spironolactone was inappropriate in 1 out of the 10 patients and could not be assessed in 1 patient, due to inadequate documentation of patient response to other HF therapy. None of the 10 patients was prescribed a potassium supplement. This could not be assessed 4 patients due to the unavailability of laboratory results.

- **ACE-Inhibitors and Angiotensin Receptor Blockers (ARBs)**: ACE-Inhibitors were appropriately prescribed in 9 out of 10 patients, and inappropriately omitted in 1 patient, who had no CI to the drug. None of the patients was prescribed ARBs.
• Beta-blockers: Only 1 out of the 10 patients was appropriately prescribed beta-blockers. On the other hand, not prescribing beta-blockers was appropriate in 3 patients because of CI (fluid retention in 2 patients and asthma in 1 patient), inappropriate in 4 patients who had no CI to the drug, and could not be assessed in 2 patients due to inadequate data.

• Digoxin: It was appropriately prescribed in 6 patients and not prescribed in 4 patients (figure, 18). Not prescribing the drug in 2 out of the 4 patients was due to suspicion of digoxin toxicity.

• Nitrates and Hydralazine: Nitrates were appropriately prescribed in 1 out of 10 patients, inappropriately prescribed in 7 patients, in the absence of indication (figure, 18). None of the patients was prescribed a nitrate-hydralazine combination as recommended in the templates.

• CCB: The use of CCB in 1 out of the 10 patients was inappropriate, because nifedipine was prescribed, whereas amlodipine is the only CCB recommended in HF.

• Oral Anticoagulants: Five out of the 10 HF patients had atrial fibrillation, which according to the templates is one of the indications to warfarin. Nonetheless, only 1 patient was prescribed warfarin, although none of the patients had CI. Aspirin was prescribed in 1 patient in an anti-platelet dose, despite no indication, the patient had no CHD.

3.2.4.2 Drug Dosing:
Dosing of CV drugs was appropriate in 75% of dosing orders (table, 31). Inappropriate dosing mainly involved ACE-Inhibitors and digoxin. Dosing could not be assessed for 2 furosemide and 1 ACE-Inhibitor regimens because the dose was not documented.
Table (31): Appropriateness of CV Drug Dosing in HF Patients:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of dosing orders in HF patients (n= 10)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total number</td>
<td>Appropriate</td>
<td>Below</td>
<td>Above</td>
<td>Could not assess</td>
</tr>
<tr>
<td>Diuretic</td>
<td>10</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Loop</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Digoxin</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nitrates</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total (%)</td>
<td><strong>28 (100)</strong></td>
<td><strong>21 (75)</strong></td>
<td><strong>4 (14)</strong></td>
<td>0</td>
<td><strong>3 (11)</strong></td>
</tr>
</tbody>
</table>

* Out of the 2 prescribed doses, 1 was prescribed for non-cardiac indication (ascites), hence excluded.

The route of administration in 2 out of the 10 prescribed furosemide dosing regimens was sub-optimal, where it should have been orally rather than intravenously, due to the absence of edema or resistant edema.

Despite that all ACE-Inhibitors complied to the recommended dosing range, none of the 9 patients was prescribed target ACE-Inhibitor doses.

3.2.4.3 Therapy Monitoring and Follow Up of Patients:

- Blood pressure, heart rate and weight: Data on monitoring therapy on admission and follow up of patients were available for 7 and 6 patients, and missing in 3 and 1 patient, respectively. BP was monitored on admission in 2 out of 7 patients only and followed up in 3 out of 6 patients. Heart rate was monitored on admission in 4 out of 7 patients only and was followed up in 4 out of 6 patients. Patient weight was not monitored neither followed up in any of the HF patients.

- Edema was monitored in 7 out of 10 patients, and data were missing for 2 patients. Edema was followed up in 3 out of 7 patients only, and data were missing for 1 patient.
Other HF signs and symptoms such as SOB, PNDs, elevated JVP were followed up in 3 out of 7 patients only, and data were missing in 1 patient.

- Monitoring of renal function was done in 4 out of 10 patients, incomplete in 2 patients, and data were missing for 4 patients. Serum potassium and sodium were monitored in 6 out of 10 patients, and data were missing for the remaining 4 patients.

- Digoxin monitoring: 2 out of the 6 patients prescribed digoxin were suspected for digoxin toxicity. The drug level was checked in 1 patient only, although it was ordered by physician in the second patient.

3.2.5 Stable Angina and HF:

3.2.5.1 Prescribing of Drugs:
The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (19). Seventy percent (70%) of CV drug use was appropriate (39% appropriately prescribed and 31% appropriately not prescribed). Conversely, 13% of drug use was inappropriate; in 4% the drug should not have been prescribed, whereas in 9% the drug was not prescribed despite no CI. Practice could not
be assessed in 17% of drug use.

The details of the evaluation of each of the CV drug groups are as follows:
- Antiplatelets: Eight patients were prescribed aspirin as recommended. The drug was inappropriately omitted in 2 patients, despite having no CI, and no alternative was prescribed, such as clopidogrel or ticlopidine.

- Beta-blockers: They were appropriately prescribed in 2 patients and omitted in 3 patients due to CI such as asthma and bradycardia. They were inappropriately omitted in 4 patients who had no CI to the drug. Not prescribing beta-blockers in 1 patient could not be assessed due to missing patient data.

- ACE-Inhibitors and ARBs: ACE-Inhibitors were prescribed in 7 patients, which was appropriate in 7 patients, while it could not be assessed in 1 patient whose data were missing. Two patients were not prescribed ACE-Inhibitors, instead they were prescribed ARBs. This was inappropriate in 1 patient who had no CI or intolerance to ACE-Inhibitors. While in the second patient there was no documentation on patient intolerance to or previous use of ACE-Inhibitors, hence the use of ARBs rather than ACE-Inhibitors could not be assessed.

- Diuretics and Potassium Supplements: A loop diuretic, furosemide, was appropriately prescribed in 8 patients. However, therapy initiation was delayed in 1 patient. Furosemide was combined with a thiazide diuretic in 1 patient and with a loop diuretic, bumetanide, in another patient (therapy duplication). Two patients were not prescribed furosemide, which was appropriate in 1 patient, who had no history or current evidence of edema. While it could not be assessed in the second patient, because data were missing. Spironolactone was prescribed in 2 patients, however, appropriate only in 1 patient. Conversely, it was omitted in 8 patients, which was appropriate in 4 patients, inappropriate in 2 patients, who had resistant edema not responding to loop diuretics, and could not be assessed in 2 patients, whose response to therapy was not documented. None of the patients was prescribed a potassium supplement, which was appropriate in 6
patients who had normal serum potassium level, and could not be assessed in 4 patients due to unavailability of laboratory results.

- Nitrates and CCB: Eight patients were prescribed nitrates. It was appropriate in 7 patients, and could not be assessed in 1 patient, whose data were missing. Nitrates were appropriately skipped in 2 patients, 1 patient was adequately managed by other medication while the second patient had CI; hypotension. CCB were prescribed in 2 patients. Amlodipine in 1 patient, which was appropriate, and diltiazem in the second patient, which is not recommended in HF.

- Digoxin: Eight patients were prescribed the drug. Only in 1 patient that digoxin prescribing was inappropriate, as it should have been deferred until therapy with ACE-Inhibitors and beta-blockers had been started. Two patients were not prescribed the drug, which was appropriate in 1 and could not be assessed in the other patient due to missing patient data.

- Lipid Lowering Drugs: Only 3 out of 10 patients had a lipid profile done, which showed abnormal lipid levels. Nonetheless, only 2 of the 3 patients were prescribed a lipid lowering drug. The choice of drug was suboptimal in 1 out of the 2 patients, where fibrates should have been prescribed instead of statins. On the other hand, 7 patients had no lipid profile, thus not using the drugs could not be assessed.

3.2.5.2 Drug Dosing:
Dosing of CV medication was appropriate in 72% of dosing orders (table, 32). In 18% of the dosing orders, the prescribed dose was below the recommended dose, which mainly involved ACE-Inhibitors, beta-blockers and lipid-lowering drugs. Dosing could not be assessed for 4 (8%) dosing regimens. These included 2 aspirin and 1 digoxin dosing regimens, because the dose was not stated, as well as 1 hydrochlorothiazide (thiazide) regimen, because of the unavailability of a consensus or a guideline dose.

The route of administration was not specified in 1 out of the 9 furosemide dosing orders.
Table (32): Appropriateness of CV Drug Dosing in SA/HF Patients:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of dosing orders in SA/HF patients (n= 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Number</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>8</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>2</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>8</td>
</tr>
<tr>
<td>ARBs</td>
<td>2</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
</tr>
<tr>
<td>Loop</td>
<td>9</td>
</tr>
<tr>
<td>Thiazide</td>
<td>1</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>1</td>
</tr>
<tr>
<td>Nitrates</td>
<td>8</td>
</tr>
<tr>
<td>CCB</td>
<td>1</td>
</tr>
<tr>
<td>Digoxin</td>
<td>7</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>3</td>
</tr>
<tr>
<td>Total (%)</td>
<td>50 (100)</td>
</tr>
</tbody>
</table>

3.2.5.3 Therapy Monitoring and Follow Up of Patients:

Data on the monitoring of CV drugs were available for 9 out of the 10 patients, except for lipid lowering therapy where it was available for 10 patients. Data on follow up of patients were available for 8 out of 10 patients, because 2 of the patients were contacted for 1 day only.

- Ischemic Pain, BP and Heart Rate: Ischemic pain was monitored in 3 out of 9 patients, because the rest of the patients had no chest pain on admission. Only 2 out of the 3 patients were followed up for ischemic pain. The third patient was contacted for 1 day only, hence no follow up notes existed. BP was monitored in 2 patients only and followed up in 4 patients. Heart rate was monitored in 6 patients and followed up in 4 patients. Data were missing for 1 patient.
• Weight and HF Signs and Symptoms (edema, SOB, PNDs, JVP): Weight was monitored on admission in 2 out of 9 patients. It was not followed up in any of the remaining 7 patients who were receiving diuretics, and data were missing for 1 patient. Edema was monitored in 7 out of 9 patients and followed up in 3 out of 8 patients. Data were missing for 1 patient. SOB, PNDs and JVP were evaluated in 6 patients. They were inadequately assessed in 2 patients (only SOB), and not evaluated in 1 patient.

• Electrolytes and Renal Function: Potassium and sodium serum levels were monitored in 7 and 6 patients, respectively. Monitoring of renal function (creatinine and urea levels) was done in 6 patients. It was inadequate (urea only) in 2 patients and not done in 1 patient.

• Lipid Lowering Therapy and Liver Transaminases: A lipid profile was obtained in 3 patients. However, it was incomplete in 2 patients were LDL and HDL were not measured. Only 1 of the 2 patients prescribed statins had liver transaminases monitored as recommended.

• Although serum digoxin level was ordered in 1 patient, it was not measured.

3.2.6 Unstable Angina and Heart Failure:

3.2.6.1 Prescribing of Drugs:
The appropriateness of drug prescribing and non-prescribing for each of the CV drug groups is illustrated in figure (20). Sixty seven percent (67%) of CV drug use was appropriate (35% appropriately prescribed and 32% appropriately not prescribed). Conversely, 13% of drug use was inappropriate; in 4% the drug should not have been prescribed, whereas in 9% the drug was not prescribed despite no CI. Practice could not be assessed in 19% of drug use.
Figure (20): Assessment of CV Drug Use in UA/HF.

The details of the evaluation of each of the CV drug groups are as follows:

- **Antiplatelets and Anticoagulants:** Aspirin was appropriately prescribed in 4 patients and inappropriately omitted in 2 patients, who had no CI. Other oral antiplatelets (i.e. ticlopidine or clopidogrel) were appropriately prescribed in 1 patient who was undergoing PCI. They were omitted in 5 patients, which was appropriate in only 1 patient, inappropriate in 2 patients and was beyond the template scope in 2 patients. None of the patients was prescribed a GP IIb/IIa inhibitor, which was appropriate in 2 patients, inappropriate in 1 patient and beyond the scope of the templates in 3 patients.

- **Warfarin:** It was appropriately prescribed in 1 patient and not prescribed in 3 patients who had no indication to the drug. Prescribing warfarin in 2 patients could not be assessed, because the patients underwent CABG, which was beyond the scope of the templates. Heparin, on the other hand, was prescribed as recommended in 3 patients. However, only in 1 patient that the duration of heparin therapy complied to the templates. The omission of heparin in 3 patients was not assessed because the patients underwent CABG, which was beyond the scope of the templates.
Chapter Six

• Opioids: Morphine was appropriately prescribed in 1 out of 6 patients, who had a continuing ischemic pain despite therapy. In this patient an adjunct antiemetic was not prescribed as recommended with opioids. Not prescribing morphine was appropriate in 4 out of the 6 patients and could not be assessed in 1 patient due to lack of documentation on patient response to therapy and ischemic pain.

• Beta-blockers: Half of the patients were appropriately prescribed beta-blockers, while the other half was not prescribed the drug despite having no CI.

• ACE-Inhibitors and ARBs: ACE-Inhibitors were appropriately prescribed in 4 out of 6 patients and inappropriately omitted in 2 patients who had no CI. No indication for ARBs existed in any of the patients, thus not prescribing the drug was appropriate.

• Diuretics and Potassium Supplements: Furosemide was prescribed in 3 out of the 6 patients, which was appropriate in 2 patients, and inappropriate in 1 patient, who had no indication for the drug. It was appropriately omitted in 3 patients who had no history or current evidence of edema. Spironolactone was appropriately prescribed in 1 patient only. It was not used in the rest of patients, which was inappropriate in 1 patient who had resistant edema despite therapy. None of the patients was prescribed a potassium supplement, which was appropriate in 4 patients and could not be assessed in 2 patients due to unavailability of serum potassium levels.

• Digoxin: The use of digoxin was appropriate in 5 out of 6 patients. Only in 1 patient that digoxin was inappropriately not prescribed, although the patient had HF symptoms, which were not relieved with other therapy.

• Nitrates and CCB: The use of nitrates and CCB was appropriate in all 6 patients. The former were prescribed in all patients, as recommended, whereas the latter were omitted in all patients in the absence of drug indication.
• Lipid Lowering Drugs: Only 1 out of the 6 patients, who had elevated TG levels, was appropriately prescribed a combination of statins and fibrates. Not prescribing the drugs was appropriate in 1 patient and could not be assessed in 4 patients because of the unavailability or incompleteness of lipid profile.

• Trimetazidine was prescribed in 1 patient, which was not recommended in UA.

3.2.6.2 Drug Dosing:
Dosing of CV medication was appropriate in 87% of dosing orders (table, 33). Only 1 out of the 3 heparin dosing regimens was appropriately prescribed. The other 2 regimens were prescribed as fixed-dose intermittent iv injection, whereas the templates recommended a weight-adjusted regimen. Furthermore, the duration of therapy of 1 regimen was not specified.

3.2.6.3 Therapy Monitoring and Follow Up of Patients:
The monitoring of therapy was assessed in 6 all patients. Whereas follow up of patients was assessed in 5 patients, because 1 patient was contacted for 1 day only.

• Ischemic pain was monitored and followed up in 4 out of the 6 patients. Similarly, BP and heart rate were monitored in only 4 patients, and followed up in 2 and 3 patients, respectively.

• Weight and HF signs and symptoms: Weight was monitored in only 1 of the 3 patients prescribed diuretics. It was not followed up in any of the patients. SOB, PNDs, and/or JVP were monitored in 5 patients. Similarly, edema status was monitored in 5 patients, however, followed up in only 1 patient.

• Electrolytes and Renal function: Electrolytes (potassium and sodium serum levels) were monitored in only 4 out of 6 patients. Moreover, only half of the patients had their renal function (serum creatinine and urea) monitored.
Table (33): Appropriateness of CV Drug Dosing in UA/HF Patients:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total number</th>
<th>Appropriate</th>
<th>Below</th>
<th>Above</th>
<th>Could not assess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heparin</td>
<td>3*</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Opioids**</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loop</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nitrates</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Digoxin</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lipid lowering</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total***</td>
<td>31 (100)</td>
<td>27 (87)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Two out of the 3 heparin infusions were inappropriate, yet not assessed in terms of below or above the recommended dose, because the prescribed regimen was a fixed-dose intermittent iv injection, whereas the recommended regimen was weight-adjusted, hence, they could not be compared.

** Opioids, not being classified as CV medication, they are stated here for their use in ischemic pain in CHD.

*** Numbers do not add up to the total sum, because they do not include the 2 (6.5%) fixed-dose heparin infusion mentioned above.

- Lipid Regulating Drugs: A lipid profile was obtained in only 2 out of 6 patients. It was not done in 3 and incomplete in 1 patient. Liver transaminases were not monitored as recommended in the 1 patient prescribed statins.

- Antiplatelets and Anticoagulants: WBC and platelet count were monitored, as recommended, in the 1 patient prescribed ticlopidine. Heparin monitoring was
inappropriate in the 3 patients prescribed the drug. PTT was measured in only 1 patient, while haemoglobin and platelets count were measured in the 3 patients. Yet, none of these indicators were measured on daily basis during heparin therapy, as recommended. Similarly, only 1 out of the 3 patients prescribed warfarin had INR monitored.

• Digoxin level was measured in 1 patient of suspected drug toxicity. It was not checked in another patient despite being ordered by the physician.

3.3 Gaps in CV Drug Use:
The evaluation of CV drug utilisation provided indications on gaps in several aspects of drug use, which could be proposed as areas for optimising practice. Generally, for all the CV medication, there is an opportunity for improvement of drug use, e.g. ACE-Inhibitors, beta-blockers, and nitrates. However, inappropriate practice was notable for some aspects of drug use more than others, these included:

• The use of intravenous drugs in terms of dose calculation, rate of infusion, and duration of therapy, specifically the dosing and monitoring of anticoagulants (in particular heparin) and antiplatelets.
• The use of lipid lowering medication (the lowest appropriately used medication).
• The use of fibrinolytics in myocardial infarction (to adjust doses to patient weight rather than the currently used fixed-dose regimen).
• The dosing of ACE-Inhibitors in terms of assuring the use of target doses, whenever tolerated.
• The choice of drugs, i.e. which agent to use from a pharmacological group, e.g. fibrates vs statins, popular ACE-Inhibitors and LMWH.
• The choice of route of administration (orally vs intravenously) in the management of acute coronary syndromes (UA and MI).
• The duration of diuretic therapy (i.e. to continue therapy even after the resolution of edema).
• The time of drug initiation to avoid delay in therapy.
In terms of monitoring therapy and follow up of patients, the following areas for improvement were noticed:

- The monitoring of weight in HF patients to assess patient response to diuretic therapy and adjust doses accordingly.
- The monitoring of antiplatelets and anticoagulants: aPTT (heparin), haematology indices (ticlopidine and tirofiban).
- Monitoring and follow up of blood pressure, heart rate, ischemic pain in CHD and HF signs and symptoms.
- The monitoring of lipid profile in all CHD patients.

It is realised that the above areas provide indications on gaps in drug use, however, more investigation is required to evaluate practice and identify inappropriate drug use. This is further discussed in the following section and chapter seven.
Discussion:

Application of the Checklists and the Templates:
The application of the templates and checklists to assess drug utilisation proved to be effective and feasible in the three study hospitals. Since the hospitals were from three different sectors, it illustrated the capacity of the templates and checklists to assess practice across the three settings, which probably suggests their applicability to other hospitals.

Validation of CV Drug Utilisation by the Study Cardiologists:
Despite the fact that the templates were developed with the consensus of the same cardiologists who validated the evaluation of drug use, yet, in a few instances, the cardiologists’ feedback from the validation process deviated from the templates. For example, although consensus was established on diabetes mellitus (DM) as not being a contraindication to the use of beta-blockers in CHD, the cardiologists considered not prescribing beta-blockers in one SA case appropriate due to uncontrolled blood glucose levels. Since the deviation from the template was minimal, it was not considered a limitation, however, it highlighted issues previously emphasised in the literature such as addressing the patients’ specific needs (Cranney et al, 2001) and the importance of physicians’ discretion in the management of diseases, which should not be overlooked in the presence of guidelines (Costantini et al, 2001).

Appropriateness of CV Drug Utilisation and Gaps in Practice:
The findings from the evaluation of CV drug utilisation are within the ranges reported in the literature, primarily ACE-Inhibitors, beta-blockers and aspirin (Pearson et al, 2001; Coll et al, 2005; Ordieres et al, 2004). However, they indicated opportunities for improvement of practice. These areas are also seen as opportunities for pharmacists’ contribution to patient care, as discussed in chapter seven.

On the other hand, the practice gaps identified counteract perceptions of some of the interviewed physicians (in chapter two), who opposed the introduction of guidelines for
the management of CHD, as they believed that the knowledge of physicians was satisfactory.

The prevalent use of heparin as a fixed-dose intermittent intravenous injection, which mainly occurred at the MOH hospital, was attributed by the cardiologists to the lack of intravenous pumps. Furthermore, the poor monitoring of aPTT during heparin therapy was due to the unavailability of laboratories kits. These two examples clearly indicate how the unavailability of resources considerably affect medical practice and impede effective use of medication. The use of LMWH can be suggested as an alternative to heparin in settings of under-developed laboratory facilities like the MOH, hence eliminate the need for monitoring, as it is not recommended with the drugs.

It is realised that the findings from the evaluation of monitoring patients, in the light of incomplete documentation in the files, could be underestimating what has actually been done. However, as there was no proof of it in the patients’ files it was considered lacking.

Interestingly, the gaps in drug use identified in this study match the drug-related areas pointed out by the interviewees, in chapter two, for further education and training of HCPs, such as the use of intravenous therapy, choice of drugs, doses and route of therapy.

Limitations:
Despite the small size of the sample, the in-depth analysis of individual patient cases uncovered an array of indications on gaps in practice and areas for improvement. Nonetheless, it is acknowledged that further investigation of the findings is needed in bigger groups of population and different settings to establish more representative data on the current drug use practices.
Chapter Seven:

Overall Discussion and Conclusion of the Thesis.

This chapter discusses the findings of the project in terms of their contribution to existing knowledge and the key research questions raised for future investigation. It presents recommendations for further building on the project and its implications for the development of the pharmacist's role in the Jordanian setting. Furthermore, the lessons learnt from conducting the research are highlighted along with addressing its limitations.

Overview of the Main Objectives of the Thesis:
The four main objectives of the research presented in this thesis have been met. First, it provided an overall view of the Jordanian health conditions and infrastructure, and identified the major health problems and issues. Second, it explored the drug utilisation processes in cardiac diseases in Jordanian hospitals. Third, it developed guidelines for the assessment of cardiovascular (CV) drug use in local settings. Finally, it evaluated CV drug use practices, identified gaps and proposed areas for practice improvement, highlighting the opportunities for pharmacists in patient care. Nonetheless, it is realised that the gaps identified only provide indications and can not be generalised to local practice. In order to obtain a representative pattern of practice, the drug use evaluation has to be carried out in bigger groups of patients. This is further addressed below when discussing the limitations of the project.

Contribution of the Thesis to Existing Knowledge:
The research, being conducted in a considerably under-investigated setting, has contributed valuable information to the existing knowledge on Jordanian health care, particularly at secondary level. It granted better understanding of the factors, which influence drug procurement and utilisation, medical practice, prescribing habits and patient care. These factors, although known to HCPs, they have not been properly addressed or documented by research yet. The project also confirmed and expanded on the few previous reports on the limited role of pharmacists in patient care in Jordan. It highlighted the limited communication between HCPs, and documented the present
continuing medical education activities and drug information sources used by physicians, pharmacists and nurses.

Furthermore, the project, to the best of the researcher's knowledge, is the first to explore the pioneering experience of clinical pharmacy practice in the army sector. Additionally, it is the first to describe the patterns of CV drug prescribing and monitoring in Jordanian hospitals. The project also tested the concept and methodology of establishing local guidelines for practice assessment, which is still a new experience in Jordan. The gaps uncovered from the evaluation drug use contributed to characterizing the Jordanian practice, which is still an unexplored area, and learning more about the opportunities to improve drug use and to develop the pharmacists' role in patient care.

Limitations of the Project and Lessons Learnt about the Research Process:

One of the important lessons that were learnt during conducting the research was the importance of possessing sensitivity to the study setting in terms of the research design and the researcher's way of approaching individuals. It was realised how the Jordanian setting was not research-oriented, particularly towards practice evaluation, audit and quality assurance measures. This was confirmed by the discontent and unfriendliness exhibited by some HCPs especially nurses upon reviewing the patients' medication charts. This was one of the limitations encountered, which emphasised the need for education to stress on the importance of conducting research, to assure staff and adopt a non-blame approach when evaluating practice.

As explained earlier the small sample size in this project limited the generalisability of its findings on practice gaps. Nonetheless, the project was designed to provide a preliminary view of CV drug use patterns and to develop a tool for practice assessment, i.e. practice evaluation was not the sole goal of the project. Therefore, proposals are made to investigate CV drug utilization in a bigger sample of patients, as discussed below.
The development of the templates did not involve pharmacists other than the researcher, which is to be considered in future work of updating and maintaining the developed templates, or even the development of local guidelines in clinical areas other than CVD. The involvement of more pharmacist aims at opening channels for inter-professional collaboration between pharmacists and physicians and affirming a multi-disciplinary approach to health policy making and patient care.

The project did not look into settings like the outpatients, because of decision of the researcher to focus on inpatient settings and the role of clinical pharmacists in secondary care level. However, practice in the outpatient settings is an area that has not been investigated yet, and must be addressed by research, especially that these settings are very important in the management of chronic diseases, including CVD.

**Future Implications for Research and Priorities for the Next Steps of Building on the Work:**

**Future Research:**
The project uncovered an array of key issues for future research, particularly in the CVD area. It is a prime time to propose strategies to enhance the management of CVD, due to the rising attention of the health authorities on the alarming levels of mortality and morbidity associated with these diseases in the Jordanian population. On the other hand, the extrapolation of the project findings to other settings and diseases generates more research questions, which are listed below:

Fist, since the project was conducted in the inpatient settings only, and indicated many deficiencies in the prescribing and monitoring of CV drugs, it raised questions about the appropriateness of practice in the busier outpatient settings. In the meantime, it is very difficult to comment on practice in the outpatient setting due to the scarcity of research. However, the lack of treatment protocols and quality assurance enforcement measures allow predicting gaps in practice. Nonetheless, this has to be investigated to enable identification of the level of inappropriate practice, the drugs and patient groups mostly
involved, and the opportunities to optimise practice in outpatients. The use of drugs at the primary/secondary interface and post discharge is another crucial area for research, as it has not been explored yet. Assuring effective transfer of care between the different settings and the appropriate use of medication by patients post-discharge is essential for the success of therapy.

Second, all the identified gaps in CV drug use are worth more investigation i.e in a bigger sample and in areas other than cardiac diseases. For instance, the evaluation of the use of intravenous medication, the appropriateness of dosing and monitoring of anticoagulation, fibrinolytics, lipid-lowering drugs, diuretics, or ACE-Inhibitors could all be proposals for future research, as well as the appropriateness of drug administration processes, nurses practices and the documentation of patient information.

Third, the successful experience of developing local guidelines for the management of cardiac diseases, as demonstrated in the thesis, encourage repeating the experience for other diseases and clinical areas. This is particularly opportune at the present time with the serious steps towards the accreditation of Jordanian hospitals executed jointly by the Jordanian MOH and the United States Agency for International Development (USAID). Recent discussions (in July 2006) with personnel from the USAID revealed the setting’s need for developing guidelines for the use of antibiotics and the management of infectious diseases. Other priority areas for the introduction of guidelines, inspired by the literature, are the management of hypertension, diabetes, dyslipidaemia, respiratory diseases and neoplasm, which are among the most prevalent diseases in the Jordanian population.

Fourth, the seriously inadequate patient counseling services and the problematic patient compliance to medical orders, as pointed out by the interviewed HCPs, call for their investigation more thoroughly, due to their importance in determining the success of disease management. Exploring the level of patient adherence to therapy in the light of the environmental, cultural and economic circumstances of the Jordanian setting would allow designing strategies to enhance compliance.
Fifth, the reported defects in communication among HCPs is also an area for investigation to determine its level and implications on patient care. Understanding the obstacles to inter- and intra-professional communication and examining the most effective strategies to enhance it are essential to tackle this issue.

Sixth, the deficiencies in public awareness on their health conditions, healthy life-style and disease management as reported in the literature illustrate the need for more exploration of their causes and the effective health education campaigns.

**Building on the work:**

Several lessons were learnt during the conduct of this project, however, an important lesson, which was repeatedly reinforced was the need of the Jordanian setting for education at all levels, i.e. senior and junior staff, administrators, practitioners and patients. Despite the fact that the concepts of evidence-based medicine, audit and quality assurance enforcement, use of guidelines, and multi-disciplinary approach to practice are known to a group of HCPs, however, they are still far from implementation in real practice. Therefore, education to endorse these important measures is believed to be one of the priority measures to build on the work that has been accomplished in this projects and previously conducted studies. Education is believed to give impetus to change the current practice and the perceptions of HCPs, especially in terms of quality assurance. Education and training of pharmacists, in particular, to qualify them for the ‘untraditional’ role as clinical pharmacists is a mandatory prerequisite to their contribution in patient care and therapy decisions. It is realised that executing these steps is a long term process, which require the cooperation and collaboration of many parties, e.g. policy makers and practitioners, the MOH, the pharmaceutical association, hospitals and universities.

As for the short term building on the work, it should logically start with establishing recognition and support to the developed guidelines and to publish the findings of the project. To achieve this goal several measures are planned, which should run parallel to each other. These include:
Chapter Seven

- To discuss the findings of the project with hospital administrators, pharmacy managers, practitioners, and pharmacists, highlighting the areas for practice improvement, and stressing on the benefits of achieving evidence-based practice, implementing quality assurance activities, disseminating guidelines, and encouraging inter-professional collaboration and multi-disciplinary approach to patient care. Furthermore, illustrate the potential role for pharmacists in assisting therapy decisions, monitoring therapy, providing drug information, educating other HCPs on medication and developing treatment protocols. Quality assurance measures should be emphasised as a measure to improve practice rather than to establish accountability and punitive actions against staff. This is believed to ameliorate the reluctance of HCPs towards these measures, which was noticed during the project.

- To participate in national and regional conferences to share the Jordanian experience of developing local guidelines and evaluating practice with other local and neighbouring settings. Moreover, to give lectures and seminars with the liaison with the Jordanian MOH, the Pharmaceutical Association, the WHO, the USAID, the faculty of pharmacy and locally at hospitals.

- To update the templates to incorporate recent evidence-based data. The study cardiologists have been already contacted and agreed on participation of the update of the templates. However, liaison with national health bodies as the MOH and Jordan FDA, the USAID and the WHO is intended to invite them to adopt and maintain the templates through panels of experts (stress on involving pharmacists and nurses).

- To propose conducting an evaluation study of CV drug use patterns in a larger group of patients to obtain a better representation of clinical practice in Jordanian hospitals. It would be valuable to conduct a before-and-after study to illustrate the effect of introducing the guidelines to the local settings. This can be expanded in the future to involve studies on the strategies effective to enhance
adherence to the guidelines and/or the cost-effectiveness of their implementation.

In addition to all of the above, several papers are in the process of being published. Among the journals targeted is the East Mediterranean Health Journal, which is known to publish on health issues in the Middle East region, hence, the findings from the project would hopefully reach to a wider range of HCPs in Jordan and the region.

The Development of the Pharmacist's Role in Jordan:

The opportunities for the professional development of the pharmacists' role are ample. The gaps identified in this study can serve as a gateway for pharmacists' participation in patient care. Examples on this involve:

1- Assuring appropriate use of drugs, through assisting physicians in therapy decisions and nurses in handling and administering medication, particularly iv medication, hence prevent medication errors.

2- Rationalising drug use and minimising waste (e.g. therapy duplication, overdosing, unnecessary medication) and advising on cheaper alternatives.

3- Promoting generic prescribing and its benefits in rationalising drug spending, particularly in the public sector.

4- Monitoring therapy and following up of patients to assure that the desired therapy outcomes are achieved.

5- Educating patients on drug use and healthy life-styles, and encouraging them to comply to therapy.

6- Organising patient care at the primary/secondary interface and assure accurate documentation of drug history, discharge medications, and pharmaceutical care plan.

7- Engaging in designing treatment protocols to standardise care and planning interventions to disseminate and implement guidelines.

Again, it is important to emphasise the need to adequately train pharmacists in the above areas to guarantee their success. Hence, convince administrators in the local settings of
the benefits of these unconventional roles of pharmacists in patient care. Eventually, this will endorse the introduction of clinical pharmacy practice and grant pharmacists the recognition among other health care professionals as primary contributors to patient care. Staff motivation and planning incentives are other measures to encourage pharmacists to take the challenges associated with their new roles, as learnt from the army sector experience of introducing clinical pharmacy training program.

Opportunities for professional development also extend to pharmacists in the primary care setting. Pharmacists in community pharmacies have a unique position, being easily approachable by the public, to assess and assist drug use in the community. The pharmacies in every community can act as sites to follow up on chronic and prevalent diseases such as hypertension, diabetes, chronic HF and CHD, to ensure appropriate patient care. Moreover, pharmacists can provide patient education, liaise with doctors, and keep accurate records of the patients’ medication. Four years ago, the pharmacies participated in a similar experience, however, only in the area of family planning and contraceptives use. It took a lot of effort and education to promote the project through seminars and workshops involving pharmacists. These were organised jointly by the WHO, the MOH and the universities. By granting honorary certificates and recognition in local conferences, pharmacies were motivated to achieve the objectives of the program. Repeating the experience with more prevalent chronic diseases is expected to be very fruitful. However, the execution requires high collaboration among many parties, primarily the MOH, the Pharmaceutical Association, the WHO, and the universities. Furthermore, the cooperation of the public is essential, and more importantly the willingness of the pharmacists to accept the high workload involved; especially that most of the community pharmacies are private businesses. Hence, planning incentives and continuing education are crucial for the success of the experience.

**Conclusion:**

Cardiovascular diseases are among the major health issues in Jordan, yet it is significantly under-investigated. The strategies for the prevention and the management
of these diseases are not well described, nonetheless, indications exist on their inadequacy. Health expenditure in Jordan is high, with hospital services and pharmaceuticals being its two major components. A wide array of factors influence the use of drugs in Jordanian hospitals and there is no active role for pharmacists in patient care at secondary level. Clinical pharmacy practice is still in its infant stages and limited to very few specialty settings.

The development of guidelines is feasible in the Jordanian settings. However, the success of their implementation and strategies to encourage adherence by health care professionals to guidelines need to be investigated.

There is an ample opportunity for the optimisation of CV drug use processes in Jordanian hospitals and the professional development of the pharmacists’ role to effectively contribute to patient care. However, adequate training of pharmacists is a prerequisite for such a role.
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-283-


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Appendices
A) The University Hospital:

Dear Sir,

I am a Jordanian pharmacist, currently pursuing PhD degree at the School of Pharmacy, University of London.

In the fulfilment of this degree, I am conducting a research which aims at the evaluation of drug use and prescribing patterns at Jordanian hospitals. Upon reviewing literature, I found that such research would be one of the very few structured attempts to describe the ongoing practices at Jordanian hospitals. Health is an issue of prime importance in our lives. A better health care service and access to this service would guarantee a better health outcome. However, in order to achieve such goal we have to evaluate the ongoing services and identify the capacities and shortcomings of the health system, to be able to determine areas that need development and recommend convenient interventions.

Drug therapy is a mainstay in medical care. International literature shows how health systems strive to provide adequate therapy to meet the continuously increasing public demands and expectations in the face of fixed budgets. Efforts are geared towards enhancing the rational and cost-effective use of drugs. This requires strict policies, co-operation of health care bodies and personnel, and effective information systems in the areas of drug use and regulation.

In developing countries the status of drug use is more critical. The systems struggle under pressures of increasing demands, seriously limited resources and drug supply, lack of updated drug information systems, and limited audit and research on drug-related services. The compromised documentation of the health system conditions has led to the lack of a reliable data-base, which can be used to plan services or at least evaluate the ongoing situation accurately.

The limited literature on health care in developing countries suggests how crucial is the need to evaluate the ongoing health care services, and optimise rational and effective delivery of service.
The research will involve:

1- Pilot stage:
Description of the Jordanian health system, the major health problems, the health care services, their delivery and coverage of population.

2- Main stage:
1- Review of drug use and prescribing patterns at hospitals from different sectors. Also, illustration of the factors that influence practices at each sector.
2- Evaluation of the hospital services of treatment, monitoring and follow-up on patients.
3- Recommendation of interventions to enhance quality of health care services, effective use of medicines, and therapy outcome.

Such a research will help answering questions as:
1- The pilot stage:
• How does the health system function? What are the major health problems? How is health care delivered? and how are drugs supplied and clinically used?

2- The main stage:
• What are the factors that influence drug use? Is clinical use of drugs rational? Is therapy monitored and followed-up effectively?
• What are the factors that determine drug supply and availability at hospitals? What factors preclude effectiveness in delivering therapy and following-up on patients? What are the constraints of the system?
• How can we increase the quality of therapy and effectively influence prescribing patterns? How can we achieve more rational and cost-effective use of medicines? How can we optimise the quality of current practices within the available system’s conditions and resources?

Answering such questions will render the process of decision making, to maximise effective and rational drug use and subsequently achieve better patient outcome, a more informed and hence a more effective process.
The research is supervised by Dr. Felicity Smith and Dr. Soraya Dhillon from the centre of pharmacy practice at the School of Pharmacy, University of London. Also, Dr. Abdullah Al-Khawad from the Faculty of Pharmacy, Petra University.

Do kindly refer to the attached protocol for a more detailed outline on the research aim, objectives and methodology. Also, you will find enclosed my curriculum vitae.

The choice of the Jordan University hospital depended on several reasons, which made the hospital an especially attractive field to conduct the study.

First, being one of the major referral hospitals in Jordan, that serve a large population will allow the coverage of wide range of health care services, drug use and prescribing patterns.

Second, being the major teaching hospital in Jordan will allow a comprehensive evaluation of drug use in teaching settings. Also, it will give an insight into the practices by the different categories of health care professionals, namely, seniors, juniors and students, unlike other hospitals. Moreover, the staff and patients will be more co-operative and receptive to the idea of conducting research, in part of supporting academic interests.

This has encouraged me to send my research protocol for your review and hopefully your support. I am strongly dedicated to fulfil my aim in conducting this research. I hope that you will help in making this ambition achievable. People in our society do deserve better health care, and there is a substantial need to enhance the quality of service and provide it in a better way.

I sincerely feel that it is the duty of every capable member in the society to work on achieving such a noble aim.

Please accept my best regards.
B) The MOH Hospital (appendix 1: continued):

Dear Sir,

I am a Jordanian pharmacist, currently pursuing PhD degree at the School of Pharmacy, University of London. In the fulfilment of this degree, I am conducting a research which aims at the evaluation of drug use and prescribing patterns at Jordanian hospitals. Upon reviewing literature, I found that such research would be one of the very few structured attempts to describe the ongoing practices at Jordanian hospitals.

Health is an issue of prime importance in our lives. A better health care service and access to this service would guarantee a better health outcome. However, in order to achieve such goal we have to evaluate the ongoing services and identify the capacities and shortcomings of the health system, to be able to determine areas that need development and recommend convenient interventions.

Drug therapy is a mainstay in medical care. International literature shows how health systems strive to provide adequate therapy to meet the continuously increasing public demands and expectations in the face of fixed budgets. Efforts are geared towards enhancing the rational and cost-effective use of drugs. This requires strict policies, co-operation of health care bodies and personnel, and effective information systems in the areas of drug use and regulation.

In developing countries the status of drug use is more critical. The systems struggle under pressures of increasing demands, seriously limited resources and drug supply, lack of updated drug information systems, and limited audit and research on drug-related services. The compromised documentation of the health system conditions has led to the lack of a reliable data-base, which can be used to plan services or at least evaluate the ongoing situation accurately.

The limited literature on health care in developing countries suggests how crucial is the need to evaluate the ongoing health care services, and optimise rational and effective delivery of service.
The research will involve:

1- Pilot stage:
Description of the Jordanian health system, the major health problems, the health care services, their delivery and coverage of population.

2- Main stage:
1- Review of drug use and prescribing patterns at hospitals from different sectors. Also, illustration of the factors that influence practices at each sector.
2- Evaluation of the hospital services of treatment, monitoring and follow-up on patients.
3- Recommendation of interventions to enhance quality of health care services, effective use of medicines, and therapy outcome.

Such a research will help answering questions as:

1- The pilot stage:
• How does the health system function? What are the major health problems? How is health care delivered? and how are drugs supplied and clinically used?

2- The main stage:
• What are the factors that influence drug use? Is clinical use of drugs rational? Is therapy monitored and followed-up effectively?
• What are the factors that determine drug supply and availability at hospitals? What factors preclude effectiveness in delivering therapy and following-up on patients? What are the constraints of the system?
• How can we increase the quality of therapy and effectively influence prescribing patterns? How can we achieve more rational and cost-effective use of medicines? How can we optimise the quality of current practices within the available system’s conditions and resources?

Answering such questions will render the process of decision making, to maximise effective and rational drug use and subsequently achieve better patient outcome, a more informed and hence a more effective process.
The research is supervised by Dr. Felicity Smith and Dr. Soraya Dhillon from the centre of pharmacy practice at the School of Pharmacy, University of London. Also, Dr. Abdullah Al-Khawad, from the Faculty of Pharmacy, Petra University.

Do kindly refer to the attached protocol for a more detailed outline on the research aim, objectives and methodology. Also, you will find enclosed my curriculum vitae.

Al-Basheer hospital is an especially attractive field to conduct this research. This is due to being the major governmental hospital in Amman, which serves large populations. Hence, the evaluation of drug use in this hospital will allow the coverage of a wide range of drug use and prescribing patterns, which will reflect the ongoing practices at the governmental sector in Amman. Moreover, the very high demand on the hospital and relatively fixed resources, will make running such research valuable to the hospital, as it aims at rationalising therapy and resources, and consequently improving patient outcome at lower costs.

This has encouraged me to send my research protocol for your review and hopefully your support. I am strongly dedicated to fulfil my aim in conducting this research. I hope that you will help in making this ambition achievable. People in our society do deserve better healthcare, and there is a substantial need to enhance the quality of service and provide it in a better way.

I sincerely feel that it is the duty of every capable member in the society to work on achieving such a noble aim.

Please accept my best regards.
C) The Private Hospital (appendix 1: continued):

Dear Sir,
I am a Jordanian pharmacist, currently pursuing PhD degree at the School of Pharmacy, University of London.
In the fulfilment of this degree, I am conducting a research which aims at the evaluation of drug use and prescribing patterns at Jordanian hospitals. Upon reviewing literature, I found that such research would be one of the very few structured attempts to describe the ongoing practices at Jordanian hospitals.

Health is an issue of prime importance in our lives. A better health care service and access to this service would guarantee a better health outcome. However, in order to achieve such goal we have to evaluate the ongoing services and identify the capacities and shortcomings of the health system, to be able to determine areas that need development and recommend convenient interventions.
Drug therapy is a mainstay in medical care. International literature shows how health systems strive to provide adequate therapy to meet the continuously increasing public demands and expectations in the face of fixed budgets. Efforts are geared towards enhancing the rational and cost-effective use of drugs. This requires strict policies, cooperation of health care bodies and personnel, and effective information systems in the areas of drug use and regulation.
In developing countries the status of drug use is more critical. The systems struggle under pressures of increasing demands, seriously limited resources and drug supply, lack of updated drug information systems, and limited audit and research on drug-related services. The compromised documentation of the health system conditions has led to the lack of a reliable data-base, which can be used to plan services or at least evaluate the ongoing situation accurately.

The limited literature on health care in developing countries suggests how crucial it is to evaluate the ongoing health care services and to optimise rational and effective service delivery.
The research will involve:

**1- Pilot stage:**
- Description of the Jordanian health system, the major health problems, the health care services, their delivery and coverage of population.

**2- Main stage:**
1- Review of drug use and prescribing patterns at hospitals from different sectors. Also, illustration of the factors that influence practices at each sector.
2- Evaluation of the hospital services of treatment, monitoring and follow-up on patients.
3- Recommendation of interventions to enhance quality of health care services, effective use of medicines, and therapy outcome.

Such a research will help answering questions as:

1- The pilot stage:
   - How does the health system function? What are the major health problems? How is health care delivered? and how are drugs supplied and clinically used?

2- The main stage:
   - What are the factors that influence drug use? Is clinical use of drugs rational? Is therapy monitored and followed-up effectively?
   - What are the factors that determine drug supply and availability at hospitals? What factors preclude effectiveness in delivering therapy and following-up on patients? What are the constraints of the system?
   - How can we increase the quality of therapy and effectively influence prescribing patterns? How can we achieve more rational and cost-effective use of medicines? How can we optimise the quality of current practices within the available system’s conditions and resources?

Answering such questions will render the process of decision making, to maximise effective and rational drug use and subsequently achieve better patient outcome, a more informed and hence a more effective process.
The research is supervised by Dr. Felicity Smith and Dr. Soraya Dhillon from the centre of pharmacy practice at the School of Pharmacy, University of London. Also, Dr. Abdullah Al-Khawad, from the Faculty of Pharmacy, Petra University.

**Do kindly** refer to the attached protocol for a more detailed outline on the research aim, objectives and methodology. Also, you will find enclosed my curriculum vitae.

The research will be conducted at several major Jordanian hospitals. The Jordan hospital was chosen to reflect the drug use practices ongoing at the private sector. Being a private hospital of an academic affiliation will make the staff and patients more cooperative and receptive to the idea of conducting research, in part of supporting academic interests.

This has encouraged me to send my research protocol for your review and hopefully your support.

I am strongly dedicated to fulfil my aim in conducting this research. I hope that you will help in making this ambition achievable. People in our society do deserve better health care, and there is a substantial need to enhance the quality of service and provide it in a better way. I sincerely feel that it is the duty of every capable member in the society to work on achieving such a noble aim.

Please accept my best regards.
D) Covering Letter to the Army Sector to Conduct Interviews with Pharmacists
(appendix, 1: continued):

Attention to: His Excellency Chairman of the Joint Chiefs of Staff,
General M. Malkawi.
Jordan Armed Forces.

Dear sir,

I am a Jordanian pharmacist currently conducting a research on drug-use in cardiac
diseases at Jordanian hospitals, in fulfilment of the requirement for PhD degree at the
University of London. The research involves description of health status of the
Jordanian population and the structure of the Jordanian health care system. The Royal
Medical Services (RMS) play a prominent role in health care in Jordan. It has gained a
wide reputation in the region for its advanced and comprehensive health care services,
which can not be overseen when discussing health care. Furthermore, RMS pioneered
the experience of clinical pharmacy practice, being the only setting where clinical
pharmacy is practised. An experience which is worth documenting. Furthermore, one of
the project’s aims is to create new roles for pharmacists in patient care and get them
more involved in their settings. This renders learning about the RMS experience in
introducing clinical pharmacy practice and services very important. Valuable lessons
could be learnt from such experience, especially when considering the introduction of
clinical pharmacy practice to other Jordanian health care settings, namely the Ministry
of Health, university and private hospitals.

Upon contacting the chief pharmacist at the RMS for information on clinical pharmacy
practice, the permission of your excellency was requested.
I will be highly appreciative for your support and cooperation by granting me the
permission to conduct interviews with clinical pharmacists at RMS in order to discuss
their experience in introducing clinical pharmacy practice and implementing its services.

Thank you in anticipation and looking forward to hearing from you soon.
Best regards,
2: Interview Guides.

The Ministry of Health (MOH):

Structure of the Health System:

- Who puts legislation to regulate health system?
- Are legislation made exclusively by the MOH? If no, ask:
  What are the other bodies that collaborate to regulate the health system?
- What are the sectors of the health system?
- What are the faces of contact between the health sectors and the MOH?

Health Problems and Population Epidemiology:

- What are the major health problems we are facing today?
- What are the government policies to face these problems?
- What are the most prevalent diseases in the Jordanian population?
- Does the patterns of disease vary among the population? If yes:
  How would you describe such variation?
- Which are the sectors of the population in most need to health services?
- How would you describe the accessibility to health services?

The Health Services:

- Could you please tell me about the health care services and programmes provided by the ministry?
- What are the types of health facilities affiliated to the ministry?
- What are the types of primary care centres available?
- What are the types of services offered by these centres?
- What about the geographical distribution of these services?
- Who is served by those?
- Coming to hospitals, how many hospitals are affiliated to the ministry?
- How big are those hospitals (no. of beds)?
- Who do they serve?
- Is it the ministry which administrates these hospitals?
- In regards to drug supply to these hospitals? Who decides what drugs to be in the hospital?
• What are the factors that influence the drug supply?
• How does the ministry evaluate the level of performance of the health facilities?
• What are the major constraints the health system is facing nowadays?

**The Health Insurance:**
• Can you tell me about the current health insurance scheme?
• Who benefits from it? What is the population coverage?
• Can you describe the prospective health insurance scheme that is planned by the ministry?
• Who will benefit from it?
• What is the aimed population coverage?
• What does it guarantee?

**The Drug Policy:**
• By how much would you estimate the drug expenditure, how much does it constitute from the health budget?
• What are the sources that supply the drug market?
• When seeking regulation of the drug market what are the issues to be considered?
• What are the bodies responsible for regulating the drug market? How do they interact?
• What are the measures taken to regulate the drug market?
• Who determines the drugs in the market? i.e. Who says we will have this drug or we don’t need that drug?
• On what basis are the decisions to accept a drug for registration and marketing made?
• What are the difficulties the ministry faces when regulating the market?
• What are the measures taken to assure the safety and effectiveness of drugs?
• What are the types of malpractice the ministry witness from personnel in the market?
• What do you think is the cause for such malpractice?
**The Drug Information Sources:**

- What are the drug information sources available?
- How do you evaluate the accuracy of these sources?
- What does the ministry do to ensure the dissemination of safe and correct drug information to public?
- How does drug advertisement take place?
- What are the ongoing training programmes adopted by the ministry to enhance the level of health system performance?

**The Pharmaceutical Association:**

**Structure of the Health System:**

- What is the part played by the pharmaceutical association in the health system?
- If I ask you to map out the pharmaceutical bodies and establishments in the society, what will your map contain?
- What are the services provided by each of these bodies?
- What are the aspects of communication among these bodies?
- How does the organisation of these bodies take place?
- What part do these bodies take in determining the drug policy and regulations?
- What are the faces of contact between the PA and the other health bodies? (ex. MOH and medical association)
- How many pharmacists are there?
- How many pharmacies are there?
- How do you evaluate the role of pharmacist in the society?
- What are the major issues that concern pharmacists nowadays?
- Pharmacists always complain of the increasing numbers of pharmacists and increasing competition in the face of limited market size and purchasing power, thus it is adversely affecting their income, how would you comment on this?
- Do pharmaceutical services meet the demand?
- What do you think is a solution for such a problem?
- What are the measures taken to enhance the role of pharmacists in serving the population?
- What are the major pharmaceutical events that take place in Jordan?
**Governmental Hospital Administrator:**

- In the beginning, would you please give me a brief idea about the hospital?
- What are the features that distinguish governmental hospitals from hospitals in other sectors in terms of services?
- Who decides the drugs to be used in the hospital? Are prescribers involved in decision making?
- What are the factors considered when making such a decision?
- What are the factors that determine drug supply?
- How does supply take place?
- Few weeks ago a local newspaper published an article which stated that a two-month drug supply to one of the governmental hospitals was consumed in three weeks?
- How would you comment on the drug use in your hospital?
- What are the drugs mostly in need?
- What are the constraints and pressures encountered by the hospital?
- What are the measures taken to deal with these problems?
- We can witness variation in prescribing trend among doctors even when treating similar cases, how are prescribing decisions made?
- What leads to such variation in trends?
- How can we judge that a doctor’s practice is more or less effective than his/her peers?
- Are there drug information services in this hospital?
- Would you please describe these services?

**Physicians:**

**The Description of the Hospital System:**

- In what aspects do hospitals from the different sectors differ?
- How does practice vary between hospitals of different sector?
- How would the variation in administration policies affect the practice?
- What are the special features that distinguish this hospital from others?
- What made you choose to work for this hospital rather than other hospitals?
- How does practice vary between doctors in hospitals and those in single-handed clinics?
• How would you describe the work load at your hospital?
• Which is the population mainly served in this hospital?
• How does patient admission take place?
• What are the major health problems we have in our society nowadays?
• Who are the members of the medical team?
• How often do medical rounds occur? How long does it usually take?
• How many patients does a medical round usually involve? Are patients of
different disease groups or similar ailments?
• Can you describe what does a medical round involve?
• What are the faces and extent of interaction among the medical team members?
  How does this vary in teaching and non teaching hospitals?
• Do medical involve physician-patient interaction? What are the faces of such
  interaction?

_The Prescribing Practices:_

• How does drug prescribing take place, is it generic or branded?
• What are the factors you take into consideration when deciding on drug therapy?
• There is a wide variety of drugs in the market, how do you choose drugs from
  among all alternatives?
• What are the system-related reasons that affect your decision?
• To what extent a patient would affect your decision? What are the patient-related
  reasons that affect your therapy decision?
• What do you think are the factors that impede you from making optimal
  decisions?
• In which situations would you change a prescribing habit?
• What are the drugs in highest demand?
• What are the drugs most likely in shortage?
• What do you think are the causes of drug shortages?
• What do you think of doctors’ use of drugs?
• What practices should be improved?
• Assume that you have prescribed drugs that were unavailable, what do you
  usually do?
• What are the most problematic drugs in terms of dosing, administration and monitoring?
• There is a big variation between physicians in prescribing practices even in treating similar conditions, what do you think are the reasons of such variation?
• What is the evidence that supports all of these different practice patterns? i.e what proves they are effective, optimum, and cost-effective?
• Do you think it is okay for variation in practice to continue? Do you think there is a need attaining a level of practice standardisation?
• Do you have treatment guidelines?
• How applicable would the introduction of treatment guidelines be?

Drug Information Sources:
• What drug information sources do you use?
• How would you evaluate the role of MRs as a drug information source?
• How often are you visited by MRs? What types of information are provided by MRs?

• What are the major problems patients face in taking their medication?
• What are the patient follow-up services available, such as monitoring of anticoagulants, antihypertensives, or diabetic patients?
• How would you evaluate the hospital services in terms of: Effectiveness-quality-comprehensiveness-cost effectiveness?
• What are the major administration and practice obstacles in our system?
• What are the major wrong practices that take place in our systems? What do you suggest to prevent them?
• What are the drug-use areas in need for training and education?
• What are the major health issues on which public awareness must be increased?

Hospital Pharmacist:
• What are the roles played by a hospital pharmacist?
• How does drug supply take place?
• How does drug dispensing take place?
• What are the drugs mostly in demand?
What are the drugs usually in shortage?
Which do you find the most problematic drugs in terms of dosing and administration?
What are the faces of interaction between you and other medical team members?
Is there an interaction between you and patients?
How does this take place?
During your practice, what are the most likely medication errors you came across?
How do you feel about the role played by hospital pharmacists?
What types of pressure do you face that you think might affect your functioning effectively?
What are the system limitations of drug supply and use?
If you were asked for a solution for such limitations what would you suggest?
How would you evaluate clinical pharmacy services?
How do you feel about presenting clinical pharmacists to Jordanian hospitals?
Do you think there is a need for such services?

Nurses:
What and how frequent are the nursing continuing education activities?
What are the drug information sources you use?
What are the drug-related areas in need for training and education?
Is there communication between nurses and pharmacists? What does it entail?
What does communication with physicians entail?
Do you participate in medical rounds? What does it involve?
What limits your functioning?
Do you provide patient counselling?

Pharmacists at the RMS in Jordan:
When was the inception of clinical pharmacy practice at the RMS hospitals?
What was the aim of introducing it?
Describe the beginning of the experience? What resources did you need?
(Funding, personnel, location).
What were the factors that supported the introduction of clinical pharmacy practice? And what were the obstacles? (Probe: financial, logistic, administrative, etc).

What are the services provided by clinical pharmacists? (Probes: participation in medical rounds, monitoring therapy, patient education, provision of drug information to HCPs etc).

How does the role of clinical pharmacists differ from that of pharmacists in the outpatient and inpatient pharmacies?

How many clinical pharmacists are there? What is the time they spend in doing their activities?

What did clinical pharmacy practice add to hospitals and medical practice? Who benefited from the implementation of services? Probes: Whether in terms of: - Drug use and prescribing practices - HCPs practices - Patient care.

How do you assess physicians practice and patient care, before and after the provision of clinical pharmacy services?

How do members of the medical team react to the presence of clinical pharmacists? What factors influence their reaction?

How do you find patients' reactions towards the presence of pharmacists in the medical team? To what extent do you think they comply to your advice on medication?

Is there a process to evaluate the effect of clinical pharmacy services (on drug use, patient awareness on medication, resource rationalisation)?

In light of your experience, what skills a clinical pharmacists should posses to function effectively?

Are there continuing education activities for pharmacists? What are they?

How do you evaluate the clinical pharmacy services currently provided? (Positive and negative issues).

What are the challenges tackled in managing clinical pharmacy staff and services? (Probe: Finance, planning, staff, workload, etc.)

What are your expectations and ambitions concerning the clinical pharmacy practice? (How do you see it going?)
How do you see the introduction of clinical pharmacy to other sectors, as the MOH, the university and the private hospitals? How applicable would this be?
Probe: why, and why not?

In light of your experience, what do you advise if we wish to introduce clinical pharmacy to other settings? What are the issues to be taken into consideration?
3: Data Collection Forms:

**Patient Data Collection Form**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal range</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>135-148 mmol/l</td>
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</tr>
<tr>
<td>K</td>
<td>3.5-5 mmol/l</td>
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<tr>
<td>Cl</td>
<td>97-110 mmol/l</td>
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<tr>
<td>FBS</td>
<td>3.9-6.1 mmol/l</td>
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<td>Random BS</td>
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<td>Urea</td>
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<td>Creatinine</td>
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<td>Triglycerides</td>
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<td>Protein total</td>
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<td>Albumin</td>
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<td>Bilirubin total</td>
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<td>Theophylline</td>
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<td>Phenytin</td>
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**Other comments:**

**Medical Procedures of Monitoring and Follow Up on Patients:**

**Patient Progress Notes:**

**Pharmaceutical Issues:**
**Data Collection Forms (continued):**

<table>
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<tr>
<th>DOTI*</th>
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<td>Duration</td>
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* DOIT: Date of inception of therapy.
4: Coding Frames (Devised for Data Entry into SPSS):

1- Patients and Type of Hospital:
Each patient will be given a number, in the order of inclusion in the study. Patient numbers will be preceded by a one digit, which indicates the type of hospital where the patient was screened:
1 = Jordan university hospital (JUH).
2 = Jordan hospital (JH).
3 = Al-Basheer hospital.
For example: first patient at the JUH, JH and Al-Basheer hospital, shall have the codes: 101, 201, 301, respectively.

2- Patient Age:
-9 = missing value.

3- Patient Gender:
1 = male.
2 = female.
9 = missing.

4- Ward:
1 = CCU only
2 = ICU only.
3 = MW only.
98 = not applicable.
99 = Missing.

5- Outcome of Stay:
0 = died.
1 = discharged.
2 = discharged upon patient’s wish.
3 = discharged to RMS.
4 = still in CCU.
5 = still on ward.
6 = still in ICU.
99 = missing.

6- Length of stay.
97 = Incomplete data.
98 = Not applicable.
99 = Missing.

7- Length of minimum stay.
98 = Not applicable.
99 = Missing.

8- Diagnosis:
1 - 9 = Cardiac signs and symptoms.
10 - 19 = Heart failure.
20 - 39 = Coronary artery diseases or coronary heart diseases. (CAD or CHD).
40 - 59 = Arrhythmias.
60 - 69 = Conduction disorders.
70 - 89 = Valvular diseases.
90 - 99 = Cardiomyopathy.
100 - 109 = Diseases of the Pericardium
110 - 119 = Diseases of the Myocardium.
120 - 129 = Diseases of the Endocardium.
130 - 139 = Pulmonary heart diseases.
140 - 149 = Metabolic heart diseases.
150 - 169 = Cardiac tumours.
<table>
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<td>Concomitant cardiac conditions.</td>
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<tr>
<td>997</td>
<td>Incomplete information.</td>
</tr>
<tr>
<td>998</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>999</td>
<td>Missing.</td>
</tr>
<tr>
<td>1</td>
<td>Atypical chest pain.</td>
</tr>
<tr>
<td>2</td>
<td>Cardiac disease signs and symptoms only. (Dyspnea, palpitation, orthopnea, syncope, PNDs, chest pain, fatigue, oedema).</td>
</tr>
<tr>
<td>3</td>
<td>ECG abnormalities only.</td>
</tr>
<tr>
<td>4</td>
<td>Cardiomegaly.</td>
</tr>
<tr>
<td>5</td>
<td>Left ventricular hypertrophy (LVH).</td>
</tr>
<tr>
<td>10</td>
<td>Heart Failure. (If not specified).</td>
</tr>
<tr>
<td>11</td>
<td>Right heart failure.</td>
</tr>
<tr>
<td>12</td>
<td>Left heart failure.</td>
</tr>
<tr>
<td>13</td>
<td>Biventricular heart failure (CHF).</td>
</tr>
<tr>
<td>14</td>
<td>High output heart failure.</td>
</tr>
<tr>
<td>19</td>
<td>Cardiogenic shock.</td>
</tr>
<tr>
<td>20</td>
<td>CAD or CHD. (if not specified).</td>
</tr>
<tr>
<td>21</td>
<td>Coronary artery stenosis.</td>
</tr>
<tr>
<td>22</td>
<td>Coronary artery aneurysm.</td>
</tr>
<tr>
<td>23</td>
<td>Coronary artery (LAD) lesions whether single vessel or multiple vessel.</td>
</tr>
<tr>
<td>24</td>
<td>Stable angina.</td>
</tr>
<tr>
<td>25</td>
<td>Unstable angina.</td>
</tr>
<tr>
<td>26</td>
<td>Myocardial infarction.</td>
</tr>
<tr>
<td>27</td>
<td>Non-Q wave MI.</td>
</tr>
<tr>
<td>28</td>
<td>MI + coronary artery aneurysm.</td>
</tr>
<tr>
<td>40</td>
<td>Arrhythmias. (If not specified).</td>
</tr>
<tr>
<td>41</td>
<td>Atrial tachyarrhythmias.</td>
</tr>
<tr>
<td>42</td>
<td>Atrial ectopic beats.</td>
</tr>
<tr>
<td>43</td>
<td>Atrial tachycardia.</td>
</tr>
<tr>
<td>44</td>
<td>Atrial flutter.</td>
</tr>
<tr>
<td>45</td>
<td>Atrial fibrillation.</td>
</tr>
<tr>
<td>46</td>
<td>Atrial fibrillation with PVC.</td>
</tr>
<tr>
<td>47</td>
<td>Supraventricular tachycardia.</td>
</tr>
<tr>
<td>48</td>
<td>Ventricular tachyarrhythmias.</td>
</tr>
<tr>
<td>49</td>
<td>Ventricular premature beats.</td>
</tr>
<tr>
<td>50</td>
<td>Ventricular tachycardia.</td>
</tr>
<tr>
<td>51</td>
<td>Ventricular fibrillation.</td>
</tr>
<tr>
<td>52</td>
<td>Torsades de pointes.</td>
</tr>
<tr>
<td>60</td>
<td>Conduction disorders.</td>
</tr>
<tr>
<td>61</td>
<td>Sinus node disease (Sick sinus syndrome).</td>
</tr>
<tr>
<td>62</td>
<td>Atrioventricular block (first, second or third degree).</td>
</tr>
<tr>
<td>63</td>
<td>Left bundle branch block (LBBB).</td>
</tr>
<tr>
<td>64</td>
<td>Right bundle branch block (RBBB).</td>
</tr>
<tr>
<td>70</td>
<td>Valvular diseases.</td>
</tr>
<tr>
<td>71</td>
<td>Mitral valve stenosis.</td>
</tr>
<tr>
<td>72</td>
<td>Mitral valve regurgitation.</td>
</tr>
<tr>
<td>73</td>
<td>Mitral valve stenosis + regurgitation.</td>
</tr>
<tr>
<td>74</td>
<td>Mitral valve prolapse.</td>
</tr>
<tr>
<td>75</td>
<td>Mitral valve prolapse + regurgitation.</td>
</tr>
<tr>
<td>76</td>
<td>Aortic valve stenosis.</td>
</tr>
<tr>
<td>77</td>
<td>Aortic valve regurgitation.</td>
</tr>
<tr>
<td>78</td>
<td>Aortic valve stenosis + regurgitation.</td>
</tr>
<tr>
<td>79</td>
<td>Tricuspid valve stenosis.</td>
</tr>
</tbody>
</table>
80 = Tricuspid valve regurgitation.
81 = Tricuspid valve stenosis + regurgitation.
82 = Pulmonary valve stenosis.
83 = Pulmonary valve regurgitation.
84 = Pulmonary valve stenosis + regurgitation.
85 = Valve replacement.

90 = Cardiomyopathy. (If not specified).
91 = Dilated cardiomyopathy (congestive).
92 = Hypertrophic cardiomyopathy.
93 = Restrictive cardiomyopathy (infiltrative).

100 = Diseases of the pericardium.
101 = Pericarditis.
102 = Acute pericarditis.
103 = Pleuro-pericarditis.
104 = Constrictive pericarditis.
105 = Effusive and constrictive pericarditis.
106 = Pericardial effusion.

110 = Diseases of the myocardium.
111 = Myocarditis.
112 = Viral myocarditis.
113 = Hypersensitivity myocarditis.
114 = Giant cell myocarditis.

120 = Diseases of Endocardium.
121 = Endocarditis.
122 = Acute endocarditis.
123 = Subacute endocarditis.
124 = Prosthetic endocarditis.

130 = Pulmonary heart diseases.
131 = Acute cor pulmonale.
132 = Chronic cor pulmonale.

140 = Metabolic heart diseases.
141 = Hyperthyroid heart diseases.
142 = Hypothyroid heart diseases.
143 = Thiamine deficiency heart diseases.

150 = Cardiac tumours.
151 = Cardiac myxoma.
152 = Rhabdomyoma.
153 = Papillary Fibroelastoma.
154 = Angioma.
155 = Fibromas.
156 = Lymphangiomass.
157 = Neurofibromas.
158 = Lymphosarcoma.
159 = Angiosarcoma.
160 = Fibrosarcomas.

170 = Congenital heart diseases.
171 = Ventricular septal defect.
172 = Atrial septal defect.
173 = Persistent ductus arteriosus.
174 = Coarctation of the aorta.
175 = Fallot’s tetralogy.

180 = Cardiac procedures and surgery.
(If not specified).
181 = Catheterization or post catheterization care.
182 = Post catheterization complications (example: haematoma).
190 = Drug related cardiac problems.
191 = Drug induced bradycardia.
192 = Digoxin toxicity.

200 = CHD + Arrhythmias. (if CHD and arrhythmias are not specified).
201 = CHD + atrial fibrillation. (When CHD is not specified).
202 = Unstable angina + atrial fibrillation.
203 = MI + Atrial fibrillation.
204 = MI + ventricular tachycardia.

215 = CHD + Cardiac arrest.
216 = MI + Cardiac arrest.

220 = CHD + HF. (If CHD are not specified).
221 = Unstable angina + HF.
222 = Stable angina + HF.
223 = MI + HF.

230 = CHD + Conduction disorders. (If CHD are not specified).
231 = Unstable angina + LBBB.
232 = MI + LBBB.
233 = CHD + LBBB. (If CHD not specified).

240 = CHD + Cardiac procedures.
241 = CAD + Catheterization.
242 = CAD + PTCA.
243 = CAD + stent or post stent care.
244 = CHD + CABG.
245 = Stable angina + catheterization or post catheterization.

246 = Stable angina + CABG.
247 = Unstable angina + Catheterization (or post catheterization).

248 = MI + stent (or post stent).
249 = MI + CABG (or post CABG).
250 = Unstable angina + non-Q wave MI + PCTA (or post PCTA).
251 = Unstable angina + CABG.
252 = Stable angina + stent or post stent.

260 = CAD + Cardiac procedures + HF.
261 = CAD + catheterization or post catheterization + CHF.
262 = CAD + CABG + CHF.
263 = CAD + HF + Stent.

270 = CHD + Arrhythmias + Conduction disorders.
271 = Unstable angina + AF + RBBB.

280 = CHF + Conduction disorders.
281 = Symptoms and signs of CHF + LBBB.
282 = CHF + LBBB.

290 = Cardiac diseases + drug-related problems.
291 = CHF + Digoxin toxicity.
292 = CHF + CHD + drug induced bradycardia.

300 = CHF + Valvular diseases.
301 = CHF + Mitral valve stenosis.
310 = CHF + Arrhythmias.
311 = CHF + Atrial fibrillation.

320 = CHF + Cardiac procedure.
321 = CHF + Catheterization or post catheterization.

330 = CHF + Cardiomyopathy.
331 = CHF + Cardiomyopathy + LBBB.

340 = Cardiomyopathy + Cardiomegaly.
341 = Cardiomyopathy + LVH.

350 = Cardiomyopathy + Conduction disorders.
351 = Heart wall injury + LBBB.

360 = Cardiac signs and symptoms + post catheterization.

370 = CAD + aneurysm.
371 = MI + aneurysm + stent

997 = No enough information.
998 = Not applicable.
999 = Missing.

* Codes are not continuous to allow the addition of any new combinations of concomitant cardiac diseases, which imparts the coding frame more capacity and flexibility.
5: Cardiovascular Drug Prescribing Regimens at the Study Hospitals.
### Appendix (5):

<table>
<thead>
<tr>
<th>CV Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Prescribed for</th>
<th>BNF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiplatelets</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>100 - 162.5 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>CHD signs/symptoms, SA, UA, MI, HF/VD</td>
<td>PO: 75-325 mg o.d.</td>
</tr>
<tr>
<td></td>
<td>325 mg</td>
<td>1-2 divided doses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>250 - 500 mg</td>
<td>o.d. - b.d.</td>
<td>PO</td>
<td>CHD signs/symptoms, SA, UA, MI, CHD/HF</td>
<td>PO: 250 mg b.d.</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>75 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>PCI, CABG</td>
<td>75 mg o.d.</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>75 mg</td>
<td>t.d.s.</td>
<td>ND</td>
<td>HF</td>
<td>300-600 mg in 3-4 divided doses</td>
</tr>
<tr>
<td><strong>Beta-blockers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>10 - 20 mg</td>
<td>b.d. - t.d.s.</td>
<td>PO</td>
<td>Cardiac diseases signs and symptoms,</td>
<td>Angina: 40 mg b.d.-t.d.s., MD: 120-240 mg. Prophylaxis post MI: 40 mg q.d.s. for 2-3 days then 80 mg b.d. Arrhythmias: 10-40 mg t.d.s. - q.d.s.</td>
</tr>
<tr>
<td></td>
<td>40 mg</td>
<td>b.d.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>25, 50, 100 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 50-100 mg o.d.</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>25 mg</td>
<td>o.d.</td>
<td>ND</td>
<td></td>
<td>PO: 50-100 mg b.d. - t.d.s.</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>6.25 - 12.5 mg</td>
<td>b.d.</td>
<td>PO</td>
<td></td>
<td>PO: 3.25 - 25 mg b.d.</td>
</tr>
<tr>
<td>Pindolol</td>
<td>2.5 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 2.5-5 mg o.d. up to t.d.s.</td>
</tr>
</tbody>
</table>


t.d.s.: three times daily. VD: Valvular diseases.
### Appendix (5):

<table>
<thead>
<tr>
<th>CV Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Prescribed for</th>
<th>BNF dosing regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-ischemic drugs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimetazidine</td>
<td>20 mg</td>
<td>o.d., b.d., t.d.s.</td>
<td>PO</td>
<td>SA, UA</td>
<td>Not stated in the BNF</td>
</tr>
<tr>
<td><strong>CCB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem</td>
<td>30 mg</td>
<td>ND</td>
<td>PO</td>
<td>CHD signs/symptoms</td>
<td>Short acting formulations: 60 mg b.d.-t.d.s. up to 360 mg. Longer acting formulations: Dilzem SR: 60, 90 mg up to 180 mg b.d. Dilzem XL: 180 mg up to 360 mg o.d. Tildiem Retard: 90, 120 mg b.d. up to 480 mg in divided doses.</td>
</tr>
<tr>
<td></td>
<td>60 mg</td>
<td>b.d., t.d.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>90 mg</td>
<td>2 capsules b.d.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>120 mg</td>
<td>o.d.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>5 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td>CHD/HF</td>
<td>5 mg up to 10 mg o.d.</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>10 mg</td>
<td>o.d.</td>
<td>ND</td>
<td>HF</td>
<td>5 mg up to 20 mg t.d.s., MR: 10 mg up to 40 mg b.d.</td>
</tr>
<tr>
<td><strong>Nitrates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISDN</td>
<td>5 mg</td>
<td>p.r.n.</td>
<td>SL</td>
<td>CHD signs/symptoms</td>
<td>SL: 5-10 mg PO: 30-240 mg o.d. in divided doses.</td>
</tr>
<tr>
<td></td>
<td>10 mg</td>
<td>b.d., t.d.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 - 40 mg</td>
<td>o.d., b.d., t.d.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISMN</td>
<td>20 mg</td>
<td>b.d.</td>
<td>PO</td>
<td></td>
<td>10, 20, 40 mg b.d. up to 120 mg in divided doses</td>
</tr>
<tr>
<td>GTN</td>
<td>5-10 mcg/min</td>
<td>CI</td>
<td>iv</td>
<td></td>
<td>iv infusion: 10-200 mcg/min. Patch: 5-10 mg every 24 hrs.</td>
</tr>
<tr>
<td></td>
<td>5-10 mg</td>
<td>o.d.</td>
<td>Patch</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Appendix (5):

<table>
<thead>
<tr>
<th>CV Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Prescribed for</th>
<th>BNF dosing regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.25, 12.5, 25, 50 mg</td>
<td>t.d.s.</td>
<td></td>
<td>Post MI: 6.25-150 mg in divided doses</td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5, 5, 10, 20 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td></td>
<td>PO: 2.5-20 mg in 1-2 doses, max 40 mg o.d.</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>5mg, 20 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 2.5-20 mg o.d., max 40 mg o.d.</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>5-20 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td></td>
<td>PO: 10-40 mg o.d.</td>
</tr>
<tr>
<td>Perindopril</td>
<td>2 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 2-4 mg, max 8 mg o.d.</td>
</tr>
<tr>
<td>ARBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>8 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>CHD, HF</td>
<td>PO: 8 mg, max 16 mg o.d.</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>40-80 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 40-80 mg o.d.</td>
</tr>
<tr>
<td>Oran anticoagulants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>1.5, 2.5, 5, 10, 20 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>CHD, HF</td>
<td>Initially 10 mg o.d. for 2 days (lower doses in elderly, abnormal LFT, below average body weight).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MD: depends on INR (usually 3-9 mg o.d.).</td>
</tr>
</tbody>
</table>

INR: International normalised ratio. LFT: Liver function test.
Appendix (5):

<table>
<thead>
<tr>
<th>CV Drug</th>
<th>Dose</th>
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<th>Prescribed for</th>
<th>BNF dosing regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parenteral anticoagulants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>5000, 10000 IU</td>
<td>stat</td>
<td>iv</td>
<td>CHD signs/symptoms,</td>
<td>Stat iv inj: 5000 -10,000 IU. Infusion: 15 -25 U/kg/hr. SC: 15000 U q. 12 hrs.</td>
</tr>
<tr>
<td></td>
<td>900-1800, 10,000 IU</td>
<td>CI over 1 hr</td>
<td></td>
<td>CHD, VD, HF</td>
<td>Intermittent iv injections are no longer recommended.</td>
</tr>
<tr>
<td></td>
<td>4000, 5000, 6000 IU</td>
<td>q.q.h.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5000 IU</td>
<td>b.d., t.d.s.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LMWH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>60 mg</td>
<td>o.d., b.d.</td>
<td>SC</td>
<td>CHD</td>
<td>SC: 1 mg/kg q. 12 hrs for minimum 2 days.</td>
</tr>
<tr>
<td></td>
<td>80 mg</td>
<td>b.d.</td>
<td>SC</td>
<td></td>
<td>Not stated in the BNF.</td>
</tr>
<tr>
<td>Tinzaparin</td>
<td>14,000 Unit</td>
<td>o.d.</td>
<td>SC</td>
<td></td>
<td>SC: 3000 U q. 24 hrs.</td>
</tr>
<tr>
<td>Certoparin</td>
<td>3000 Unit</td>
<td>o.d.</td>
<td>SC</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac glycosides</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.0625, 0.125, 0.25 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>HF, VD, UA, CHD/HF, CHD/arrhythmias</td>
<td>PO: 0.0625- 0.5 mg o.d.</td>
</tr>
<tr>
<td><strong>Antiarrhythmics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>200-400 mg</td>
<td>o.d., b.d., t.d.s.</td>
<td>PO</td>
<td>CHD, HF, AF with CHD or HF</td>
<td>PO: 200 mg o.d.-t.d.s. iv infusion: 5 mg/kg over 20-120 min, max 1.2 g in 24 hrs.</td>
</tr>
<tr>
<td></td>
<td>300 mg</td>
<td>CI over 1 hr q. 8 hrs</td>
<td>iv</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AF: Atrial fibrillation. CI: Continuous infusion. IU: International units. PO: Oral. q.: Every. q.q.h.: Every four hours. SC: Subcutaneous.
## Appendix (5):

<table>
<thead>
<tr>
<th>CV Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Route</th>
<th>Prescribed for</th>
<th>BNF dosing regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diuretics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>CHD, HF, LVH, VD, Cardiomyopathy</td>
<td>PO: 20-40 mg o.d. up to 80 mg o.d. in resistant edema or more. iv injection: initially 20-50 mg.</td>
</tr>
<tr>
<td></td>
<td>40-60 mg</td>
<td>stat</td>
<td>iv</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 mg</td>
<td>o.d., b.d., t.d.s.</td>
<td>PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>80 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>25, 50 mg</td>
<td>o.d.</td>
<td>PO</td>
<td>HF</td>
<td>PO: 25 mg o.d.</td>
</tr>
<tr>
<td></td>
<td>100 mg</td>
<td>in 1-2 divided doses</td>
<td>PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>12.5-25 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td>HF</td>
<td>Not stated in the BNF</td>
</tr>
<tr>
<td><strong>Lipid-lowering</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>10 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td>CHD signs/symptoms, CHD</td>
<td>PO: 20- 80 mg o.d., max. 10 mg if combined with fibrates</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20 mg</td>
<td>in 1-2 divided doses</td>
<td>PO</td>
<td></td>
<td>PO: 10-40 mg o.d.</td>
</tr>
<tr>
<td>Atrovastatin</td>
<td>20 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 10 -40 mg o.d., max 80 mg o.d.</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20, 40 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>PO: 20-40 mg o.d., up to 40 mg b.d.</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>600 mg</td>
<td>o.d., b.d.</td>
<td>PO</td>
<td></td>
<td>PO: 600 mg b.d.</td>
</tr>
<tr>
<td>Etofibrate</td>
<td>500 mg</td>
<td>o.d.</td>
<td>PO</td>
<td></td>
<td>Not stated in the BNF</td>
</tr>
</tbody>
</table>
6: Covering Letters to Establish Consensus on the DUE Templates.

A) Letter sent in the First Round:

Dear Doctor,

Kindly find attached the templates on the management of the following diseases in adult patients:
1- Chronic stable angina (SA).
2- Unstable angina and Non-ST segment Elevation Myocardial Infarction (UA/NSTEMI).
3- Myocardial infarction (MI).
4- Heart failure (HF).

The templates were developed on the basis of the most recent guidelines issued by the ACC/AHA and ESC on the management of the above diseases. The use of these guidelines was agreed upon our previous discussions, as well as by other cardiology consultants in Jordan. Other guidelines such as the New Zealand guidelines for the management of HF, and the National Cholesterol Education Program (NCEP/ATP III) on management of hyperlipidaemia were used to complement the templates, where seen necessary. Moreover, the British National formulary (BNF) was used for information on drug dosing and contraindications.

These templates will be reviewed by several cardiology consultants in Jordan. The goal is to develop templates for the management of SA, UA/NSTEMI, MI, and HF, which will later be used in the evaluation of drug use and Jordanian practice in the management of the above diseases at university, private and MOH hospitals.

Your efforts in evaluating the templates in the light of your clinical expertise shall be highly appreciated. It is important for the following to be considered:

1- Clarify your agreement or disagreement with the guideline recommendations.
2- Assess whether the templates are applicable in the Jordanian hospitals, taking into consideration the limitations and circumstances at your local setting.

3- Explain, whenever applicable, the reasons why a guideline recommendation is not acceptable or can not be locally applied (whether in terms of drug availability, use, therapy monitoring, or follow up on patients).

Again, your efforts are highly considered. Any comments and suggestions are welcomed and will be incorporated into the templates.

Many thanks.

B) Letter sent in the Second Round:

Dear Doctor,

I would like to thank you for your participation in this project and your efforts in reviewing the templates on the management of ischemic heart diseases and heart failure.

In reference to the e-mail sent to you on September 4th 2003, most of the templates were agreed by all the cardiologists participating in the project. However, feedback from the previous round generated some issues for further processing, these included:

1- Requests for clarification of ambiguous wording and some guideline recommendations.
2- Addition of information to the templates.
3- Disagreement with some guideline recommendations.

To progress the work our objective is to resolve these issues and have the templates agreed by all the participating cardiologists.

For this purpose, please find attached the following documents for each of the four templates on stable angina, unstable angina, myocardial infarction and heart failure:
I- A list of all the issues raised by all the cardiologist on the template. It summarizes:

a - The ambiguous wording or guideline recommendations as stated in the templates you previously received in round one, along with your enquiry.

b- The additions to the templates.

c- The disagreement with the guidelines’ recommendations; illustrating:

1- The disapproved guideline recommendation as they were stated in templates you previously received.

2- The disagreement raised by the cardiologist and its rationale.

3- The feedback from other cardiologist regarding the same recommendation (feedback is anonymised).

II- Copies of sections from the guidelines pertaining to:

1- The ambiguous wording or recommendations, for which you requested a clarification.

2- The information added to Templates.

3- The disapproved guideline recommendations.

Please notice the objectives when assessing the following:

1- Additions to template:

**Objective:** Assess the added information and express your agreement or disagreement with its acceptability and applicability in your local setting.

In case you agree with the information, kindly state the evidence which supports it if available (or in the light of your clinical experience).

If you disagree, then state the reason of disagreement (e.g. whether it is related to resources, patients, inadequate scientific evidence, etc.).

2- Disapproved guideline recommendations:

**Objective:** Re-assess the recommendations in the light of the enclosed guideline sections and feedback from other cardiologists.

Please state clearly if you:

1- Agree with the guideline recommendation.
2- Agree with both the guideline recommendations and alternative practice suggested by the disagreeing physician, i.e. they both form more than one acceptable option for practice.

3- Disagree with the guideline recommendation. If so please state the following:
   a- Alternative practice and the evidence supporting it (or in the light of your clinical experience).
   b- Rationale for disagreement.

In order to help you locate the sections of guidelines relevant to the raised issues =>
You will find a number to the right of each issue in question listed in the enclosed list (item I), which will match a number in green on the page of the corresponding guideline section.

How to give your feedback?
You can reply by either:
1- E-mailing your assessment and comments to: danadarwish@hotmail.com, Or
2- Writing down your assessment and comments on the enclosed documents, and I shall arrange for their collection from you. (Please e-mail me regarding which method is more convenient).

I will be looking forward to hearing your comments soon, and will be appreciative if you send a confirmation of receipt of this package.

Best Regards.
7: Cardiologists’ Feedback from the First Round.

A) The Template for Chronic Stable Angina:

<table>
<thead>
<tr>
<th>Guideline-based Drug use Criteria</th>
<th>Feedback category</th>
<th>Cardiologists’ feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol 10 mg/day RC</td>
<td>RC</td>
<td>What is the dose range for bisoprolol?</td>
</tr>
<tr>
<td>It is not recommended to switch from one nicotinic acid preparation to another. RC</td>
<td>RC</td>
<td>Why? Justify criteria.</td>
</tr>
<tr>
<td>Metoprolol 50-200 mg twice daily. D</td>
<td>D</td>
<td>Metoprolol dose is too high</td>
</tr>
<tr>
<td>Avoid short-acting dihydropyridines in CHD. D</td>
<td>D</td>
<td>Short acting dihydropyridines can be prescribed in CHD in combination with beta-blockers.</td>
</tr>
<tr>
<td>Diltiazem: Immediate release: 30-80 mg q.d.s. Slow release: 120-320 mg o.d. D</td>
<td>D</td>
<td>Change dose to: Immediate release: 30-60 mg t.d.s. slow release: 200-300 mg o.d.</td>
</tr>
<tr>
<td>Trimetazidine, Ranolazine, and L-carnitine are metabolic agents of anti-anginal effect in some patients. D</td>
<td>D</td>
<td>Drugs were not approved for use as anti-anginal agents.</td>
</tr>
<tr>
<td>Avoid Dipyridamole. D</td>
<td>D</td>
<td>Use Dipyridamole if Aspirin is contraindicated.</td>
</tr>
<tr>
<td>Clinical experience with LMWH is still limited D</td>
<td>D</td>
<td>Experience with LMWH in SA is good and they are used in ACS.</td>
</tr>
</tbody>
</table>

### B) The Template for Unstable Angina/ Non-ST- Segment Elevation Myocardial Infarction:

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists' feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRIC trial → Dalteparin showed unfavourable trends over Heparin in UA/NSTEMI.</td>
<td>RC</td>
<td>What are the unfavorable trends associated with dalteparin?</td>
</tr>
<tr>
<td>Choice of beta-blockers: Initial choice agents include propranolol, metoprolol and atenolol.</td>
<td>RC</td>
<td>Which agent to choose?</td>
</tr>
<tr>
<td>A</td>
<td>Negative interaction exists between clopidogrel and lipophilic statins such as atrovastatin and simvastatin → Avoid concomitant use (give statins in the evening).</td>
<td></td>
</tr>
<tr>
<td>If allergy to morphine → Give meperidine HCl.</td>
<td>D</td>
<td>Use pethidine instead of morphine (to avoid respiratory depression).</td>
</tr>
<tr>
<td>Heparin should be given in a weight adjusted regimen: iv bolus 60-70 U/kg (max 5000 U) followed by infusion: 12-15 U/kg/hr (max 1000 U/hr), titrated to aPTT 1.5-2.5 times control.</td>
<td>D</td>
<td>Routine practice for iv heparin infusion is 5000 IU q.q.h.</td>
</tr>
</tbody>
</table>

A: Addition. D: Disagreement. RC: Request clarification. q.q.h: every four hours.
### C) The Template for Myocardial Infarction:

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists' feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use LMWH along with fibrinolytics.</td>
<td>RC</td>
<td>Use of LMWH in MI?</td>
</tr>
<tr>
<td>Give ACE-I to all patients within the first 24 hours, particularly if experiencing HF or low EF, in the absence of contraindications or hypotension.</td>
<td>RC</td>
<td>The time to initiate ACE-Inhibitors in the acute phase?</td>
</tr>
<tr>
<td>If risk for recurrent ventricular fibrillation is high ➔ Give iv lidocaine.</td>
<td>RC</td>
<td>What is the evidence on use of lidocaine?</td>
</tr>
<tr>
<td>In right ventricular Failure: Administer fluid loading ➔ initially rapid administration of 200 ml in 10 min. To maintain ventricular preload ➔ Give infusion of 1-2 L normal saline in first few hours then 200 ml/hr thereafter.</td>
<td>A</td>
<td>If iv fluids fail give Dobutamine infusion.</td>
</tr>
<tr>
<td>Continue administration of ACE-Inhibitors for at least 4-5 years even in the absence of ventricular dysfunction.</td>
<td>A</td>
<td>ACE-Inhibitors could be given indefinitely.</td>
</tr>
<tr>
<td>Heparin Regimen: Intravenous infusion: 12 U/kg with a max of 1000 U/hr for 24-48 hours.</td>
<td>A</td>
<td>Give heparin as intermittent iv infusion.</td>
</tr>
<tr>
<td>Give morphine: slow iv injection 4-8 mg with additional doses of 2 mg at 5 min intervals until pain is relieved.</td>
<td>D</td>
<td>Use a lower morphine dose of 2-5 mg.</td>
</tr>
<tr>
<td>In cardiogenic shock use dopamine 2.5-5 mcg/kg/min.</td>
<td>D</td>
<td>Use a higher dopamine dose.</td>
</tr>
<tr>
<td>Captopril dose: initially 6.25 mg, increased over several weeks up to 150 mg/day (if tolerated) in divided doses</td>
<td>D</td>
<td>Initial dose: 6.25 mg then 12.5 mg PO b.d. - t.d.s.</td>
</tr>
</tbody>
</table>
**Myocardial Infarction (continued)**

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists’ feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do not give dihydropyridines unless there is a clear indication (no evidence on improving prognosis post MI).</td>
<td>D</td>
<td>Dihydropyridines should be given with beta-blockers</td>
</tr>
<tr>
<td>Fluvastatin initial dose 20 mg.</td>
<td>D</td>
<td>Initial dose 40 mg.</td>
</tr>
<tr>
<td>Routine use of clopidogrel along with aspirin following reperfusion therapy is not recommended in secondary prevention.</td>
<td>D</td>
<td>Advised referring to PCI-CURE trial for routine use of clopidogrel.</td>
</tr>
<tr>
<td>If sinus bradycardia accompanied by severe hypotension ➔ Give iv atropine initially 0.3-0.5 mg, repeated up to total of 1.5-2 mg).</td>
<td>D</td>
<td>Use a higher initial dose of 1 mg.</td>
</tr>
</tbody>
</table>

### D) The Templates for Heart Failure:

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists’ feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start diuretics at low dose, then up-titrates until urine output increases and weight decreases by 0.5-1 kg/day. Avoid volume depletion or retention</td>
<td>RC</td>
<td>Requested elaboration on the statement “avoid volume depletion or retention”.</td>
</tr>
<tr>
<td>If signs of fluid retention exist ➔ Maintain diuretic dose and improve end-organ perfusion.</td>
<td>RC</td>
<td>How to improve end-organ perfusion?</td>
</tr>
<tr>
<td>Give ACE-Inhibitors with caution in unstable HF.</td>
<td>RC</td>
<td>Definition of unstable HF?</td>
</tr>
<tr>
<td>If azotemia or serum creatinine levels increase with ACE-Inhibitors in the presence of fluid retention ➔ Maintain ACE-Inhibitor therapy and encourage patient to tolerate mild to moderate degrees of azotemia.</td>
<td>RC</td>
<td>Requested elaboration on the statement “encourage patient to tolerate mild to moderate degrees of azotemia”.</td>
</tr>
<tr>
<td>Initiation of Digoxin</td>
<td>RC</td>
<td>How to initiate Digoxin therapy?</td>
</tr>
<tr>
<td>Spironolactone can not yet be recommended in mild to moderate HF.</td>
<td>E</td>
<td>Spironolactone in practice is commonly used in mild HF, despite that trials uses it only for severe HF.</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Digoxin is contraindicated in renal failure.</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Indications of warfarin in HF: dilated cardiomyopathy, aneurysm, LV dilatation.</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>Carvedilol maybe preferred in DM patients with frequent episodes of hypoglycemia.</td>
</tr>
</tbody>
</table>
### Heart Failure (continued):

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists’ Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start beta-blockers with short acting agents (metoprolol) during the first 2-3 days. If well tolerated, switch to long acting agent (bisoprolol) once daily and up-titrate the dose.</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

Give angiotensin receptor antagonists (ARBs) if → intolerance to ACE-Inhibitors. | A | Add valsartan to the templates. |

Telmisartan: Initial dose: not stated in BNF. | A | Initial dose of Telmisartan: 20-40 mg. |

Give ACE-Inhibitors with caution in severe generalized atherosclerosis, or peripheral vascular diseases. | D | Disagreed with criteria. |

Captopril maintenance dose 25 mg 2-3 times daily. | D | Disagreed with twice daily dosing. |

Give combination of hydralazine and ISDN if → Intolerance to ACE-Inhibitors due to hypotension or renal insufficiency. | D | Disagreed with criteria, stating that hypotension can also occur with hydralazine and nitrates. |

Use amiloride in HF. | D | Disagreed with criteria, stating there was no evidence on use of amiloride in HF. |

If ventricular arrhythmia is asymptomatic → Do not treat. | D | Disagreed with criteria, stating that most physicians will use beta-blockers in CHF especially with ventricular tachycardia even if asymptomatic. |
### Heart Failure (continued):

<table>
<thead>
<tr>
<th>Guideline-based DUE criteria</th>
<th>Feedback category</th>
<th>Cardiologists' feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>In refractory end-stage HF: Give nitrates and hydralazine if ACE-Inhibitors or beta-blockers are intolérated.</td>
<td>D</td>
<td>Disagrees with the criteria.</td>
</tr>
<tr>
<td>Give ARBs with caution in:</td>
<td>D</td>
<td>Disagreed with taking caution when using ARBs with aortic or mitral valve stenosis, and asked to specify renal artery stenosis as a bilateral one.</td>
</tr>
<tr>
<td>a- Renal artery stenosis.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b- Aortic or mitral valve stenosis.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c- Obstructive hypertrophic cardiomyopathy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARBs are not as effective as ACE-Inhibitors, and are likely to produce hypotension and renal insufficiency.</td>
<td>D</td>
<td>Disagrees with criteria.</td>
</tr>
</tbody>
</table>

8: Lists of Issues Sent to the Panel in the Second Round for Further Assessment:

The following two lists are shown for illustration purposes. However, a total of 12 lists were prepared (3 lists for each of the four templates). The cardiologists’ identity was anonymous, they were denoted as A, B, and C.

List 1: Cardiologists’ Feedback on the Template for the Management of Chronic Stable Angina:

I- Requests for Clarification of Wording or Guideline Recommendations:
1- Bisoprolol 10 mg/day
Enquiry: The range for Bisoprolol dose.

2- It is not recommended to switch from one nicotinic acid preparation to another.
Enquiry: Justification of the above sentence.

II- Addition to the Template:
Addition: Diltiazem dose for intermediate-release formulations 90-120 mg twice daily.

III- Disagreement with the Guideline Recommendations:
1- Dosing of B-blockers:
   Metoprolol 50-200 mg twice daily. (ACC/AHA, 2002)
Physician A: stated Metoprolol dose was too high.
Physicians B + C: Agreed with recommended dose.

2- Calcium channel blockers:
Avoid short-acting dihydropyridines in CHD.
Physician B: states that short acting dihydropyridines can be prescribed in CHD in combination with b-blockers.
Physician A + C: Agreed with recommendation.
3- Dosing of CCB:

Diltiazem
Immediate release: 30-80 mg 4 times daily
Slow release: 120-320 mg once daily. (ACC/AHA, 2002)

Physician A: Suggested changing dose of Diltiazem (immediate release) to 30-60 mg three times daily, and (slow release) as 200-300 mg once daily. Stating that doses should match those available in Jordanian market.
Physicians B + C: Agreed with recommended dose.

4- Other Anti-anginal Agents:

Trimetazidine, Ranolazine, and L-carnitine: Metabolic agents of anti-anginal effect in some patients. (ACC/AHA, 2002)

Physician B: did not approve of use of the above anti-anginal agents.
Physician A + C: Agreed with statement.

5- Avoid Dipyridamole. (ACC/AHA, 2002)

Physician B: stated use of Dipyridamole in stable angina if Aspirin is contraindicated.
Physicians A + C: Agreed with guideline recommendation.

6- Clinical experience with LMWH is still limited. (ACC/AHA, 2002)

Physician B: did not approve of this statement, stating that experience with LMWH in SA is good and that they are used in ACS.
Physicians A+ C: Agreed with statement.
List 2: Cardiologists’ Feedback on the Template for the Management of Unstable Angina and Non-ST- Segment Elevation Myocardial Infarction

I- Request of Clarification of wording or guideline recommendations:

1- Anticoagulation therapy:

FRIC trial ➔ Dalteparin showed unfavourable trends over Heparin in UA/NSTEMI. (ACC/AHA, 2002)

Request: More elaboration on unfavourable trends of Dalteparin over Heparin as stated in the FRIC study.

II- Additions to the Templates:

Addition: There is negative interaction between Clopidogrel and lipophilic statins such as Atrovastatin and Simvastatin ➔ Avoid giving both at the same time (give statins in the evening).

III- Disagreement with the Guideline Recommendations:

1- Morphine Sulfate:

If allergy to morphine ➔ Give Meperidine Hcl. (ACC/AHA, 2002)

Physician B: stated that Pethidine is extensively used in their setting to avoid respiratory depression.

Physicians A + C: Agreed with recommendation.

2- Dosing of Anticoagulant Therapy:

Heparin: Weight adjusted regimen. iv bolus 60-70 U/kg (maximum 5000 U) followed by Infusion: 12-15 U/kg/hr (maximum 1000 U/hr), titrated to aPTT 1.5-2.5 times control. (ACC/AHA, 2002)

Physician B: stated that routine practice for iv infusion of heparin in their hospital is 5000 IU every four hours.

Physicians A + C: Agreed with recommendation.
9: Results From Establishing Consensus and the Development of the Templates.

A) CV Drug Use Criteria Obtained From the Literature to Complement the Guidelines:

a- Dosing of captopril in SA: The dose was not specified in neither the guidelines nor the BNF. The literature stated a dose of 25 mg BID-TID, up to 150 mg daily (if tolerated) in divided doses (Arnaout et al, 2003; Steffensen et al, 1995; Just et al, 1993; Akhras and Jackson, 1991) (SA template, pp: 356).

b- Justification of the guideline recommendation “Do not switch between different nicotinic acid preparations”: The different sustained-release preparations were reported to exhibit considerable variations in terms of pharmacokinetics, efficacy, safety profile and adverse drug reactions (Pieper, 2003; Pieper, 2002) (MI template, pp: 399).

c- Use of ACE-Inhibitors in MI patients: The guidelines recommended giving ACE-Inhibitors to all MI patients within the first 24 hours, particularly patients with HF or low ejection fraction (EF). The literature elaborated more on the MI patient groups who particularly should receive ACE-Inhibitors. These were high risk patients with previous or anterior MI, elevated heart rate, DM, or HTN (Franzosi et al, 1998) (MI template, pp: 393).

d- Use of beta-blockers post MI:
I- Dose of carvedilol: The guidelines recommended carvedilol post MI without stating a dose. The dose in the BNF was indicated for the management of angina rather than the prophylaxis post MI. The CAPRICORN trial (2001), a multi-centre, randomized, placebo-controlled trial, involving almost 2000 patients, reported the effectiveness of carvedilol post MI at a dose of initially 6.25 mg BID increased to a maximum of 25 mg BID over 4-6 weeks if there were no adverse effects (MI template, pp: 396).
II- The guidelines recommended giving beta-blockers post MI without differentiating between beta-blocker agents (cardioselective, non-selective, and agents with intrinsic
sympathomimetic activity). A systematic review of randomized controlled trials on beta-blockers use post MI recommended avoiding agents with intrinsic sympathomimetic activity, because they were associated with a decrease in mortality reduction (Freemantle et al, 1999) (MI template, pp: 396).

e- Dose of verapamil post MI: No dose was stated in the guidelines. In several clinical trials the dose of 120 mg BID-TID was shown to be beneficial post MI (Hansen et al, 1997; Jespersen, 1993; DAVIT II, 1990; DAVIT trial, 1984) (MI template, pp: 397).

f- Routine use of clopidogrel along with aspirin following reperfusion therapy: The guidelines did not recommend routine use of clopidogrel in prophylaxis post MI. The following statement was added to the templates upon review of clinical trials on use of dual antiplatelet therapy (aspirin and clopidogrel) in ACS patients (e.g PCI-CURE and CREDO trials) and physicians' request: “Current evidence supports dual antiplatelet therapy for long-term treatment (at least 12 months) in patients with ACS after PCI, after which Aspirin is continued indefinitely. Longer-term clopidogrel should be considered based on patient risk” (Jneid et al, 2003). The present literature does not highlight dual antiplatelet therapy in ST-segment elevation MI (including those undergoing PCI)” (MI template, pp: 396).

B) CV Drug Use Criteria Added to the Templates:

The cardiologists suggested adding the following information to the templates based on their clinical experience. Supporting evidence is stated, whenever available:

a- Dobutamine infusion in right ventricular infarction when fluid infusion fails: The guidelines did not state an alternative if fluid infusion fails. The physicians suggested an infusion rate of 2-15 mcg/kg/min (MI template, pp: 389).

b- Dosing of beta-blockers in heart failure: The guidelines recommended administering beta-blockers at an initial dose, then gradually up-titrating the dose of the same agent over a period of time. The suggested Jordanian practice is to start with a short acting
beta-blocker (e.g. metoprolol), and if well-tolerated, to switch to a long acting agent (e.g. long-acting metoprolol, carvedilol or bisoprolol). This was suggested as an alternative practice to that stated in the guidelines (HF template, pp: 413).

c- Dosing of intermediate-release diltiazem: The guidelines did not state a dose for the intermediate-release diltiazem formulation. The panel agreed on a dose of 90-120 mg twice daily (SA template, pp: 352).

d- Indications to prescribing warfarin in HF to prevent thromboembolic events: In addition to the indications stated in the guidelines, the following were added: aneurysm, dilated cardiomyopathy and advanced left ventricular dysfunction, especially if a thrombus is detected (HF template, pp: 420).

e- Initial dose of telmisartan in the management of HF: No dose was stated in the BNF or the guidelines. The suggested initial dose was 20-40 mg (HF template, pp: 418).

f- Target dose of valsartan in HF: The dose was not stated in the BNF. The panel agreed on a dose of 160 mg twice daily (HF template, pp: 418), which was proven effective in the VALHEFT trial (2001).

g- Dose of trimetazidine in SA: No dose was stated in the guidelines or the BNF. The panel suggested a dose of 20 mg three times daily, which effectiveness has been proved (Manchanda, 2003; Hanania et al, 2002; Szwed et al, 2001; McClellan and Plosker, 1999; Levy et al, 1995) (SA template, pp: 355).

h- Use of carvedilol in CHD patients with DM: It was suggested as the beta-blocker of choice. Evidence has been established on the favourable effects of carvedilol on insulin sensitivity (Jacob et al, 1996; Jacob et al, 1998) (HF template, pp: 414).

i- Mode of heparin infusion in MI: The mode of infusion was not specified in the guidelines. One cardiologist suggested the use of intermittent infusion, while, the other two cardiologists supported continuous infusion. Current scientific evidence supported continuous infusion, because it was associated with reduced rates of haemorrhage.
(Gallus, 1989). Furthermore, it allowed immediate lowering of the plasma heparin level in case of complications. Besides, the normalization of clotting time was attainable in a considerably less time than with the intermittent injections (MicroMedix, 2003) (MI template, pp: 387).

j- Use of LMWH in MI as an adjunct to fibrinolytic therapy: The guidelines briefly stated the use of LMWH in MI and the supporting clinical trials, without recommending a dosing regimen. The panel agreed on the enoxaparin dose used in the ASSENT-3 trial (2001) of 30 mg iv bolus followed by SC injection of 1 mg/kg every 12 hours (MI template, pp: 387).

Additions dismissed due to lack of evidence, or disagreement of the panel included avoiding concomitant administration of lipophilic statins (e.g. simvastatin or atorvastatin) and clopidogrel due to significant clinical interaction. Also, considering renal failure as a contraindication to digoxin.

C) Consensus CV Drug Use Criteria “Jordanian Practice”: Guideline-derived criteria unanimously disapproved by the panel were modified or substituted with the alternative Jordanian practice, as explained below:

a- Use of nitrates and hydralazine in HF patients intolerant to ACE-Inhibitors due to hypotension: One of the cardiologists argued that the nitrates and hydralazine combination also will reduce BP and cause hypotension. However, another stated that patients’ response to different medications varies i.e if a patient suffers hypotension with ACE-Inhibitors it is not necessarily to occur with nitrates and hydralazine. The panel agreed to amend the guideline statement to “Give combination of hydralazine and ISDN very cautiously in low doses if intolerance to ACE-Inhibitors due to hypotension” (HF template, pp: 417).

b- Atropine dose in sinus bradycardia in acute MI: The panel approved of using a higher dose than that in the guidelines; starting at 0.6-1 mg and repeated up to a total of 2 mg or (0.04 mg/kg) (MI template, pp: 391).
**c- Dosing of immediate and slow-release diltiazem:** Doses were changed to match the formulations available in Jordan. These were 30-60 mg 3 times daily for the immediate release, and 200-300 mg once daily for the slow-release formulation (SA template, pp: 352).

**d- Dopamine dosing in cardiogenic shock during acute MI:** The guidelines recommended giving dopamine 2.5-5 mcg/kg/min and considering additional dobutamine 5-10 mcg/kg/min to maintain SBP > 90 mmHg. The Jordanian panel modified the dopamine dosing regimen to an initial dose of 2.5-5 mcg/kg/min then gradual up-titration to 15-20 mcg/kg/min (MI template, pp: 390).

**e- Treatment of asymptomatic ventricular arrhythmia in HF patients:** The guidelines recommended not to treat them, while the panel agreed on leaving management to physician’s discretion (HF template, pp: 421).

**D) CV Drug Use Criteria for which No Consensus was Reached (The Gold Standards):**

The guideline-derived DUE criteria for which disagreement sustained among the panel members were included in the templates as the “gold standard”. These were as follows:

**a- Heparin infusion in UA:** The MOH cardiologist agreed with the guideline recommendations on weight-adjusted heparin regimen, yet stated that using a fixed-dose heparin infusion or iv injection of 5000 IU every 4 hours was a routine practice in the MOH hospital. The cardiologist explained that it was difficult to abide by the guidelines due to difficulties in weighing patients, calculating doses and obtaining laboratory results of aPTT every 6 hours (UA template, pp: 375).

**b- Use of lidocaine in the management of ventricular arrhythmia post acute MI:** The guidelines recommended giving iv lidocaine if there was a high risk for recurrent ventricular fibrillation post MI. The university cardiologists stated using amiodarone in such cases, whereas, the other 2 panel members agreed on using lidocaine. The guideline recommendation was not amended (MI template, pp: 391).
e- Use of pethidine for analgesia in ACS: The MOH cardiologist stated that pethidine was used by junior doctors to avoid respiratory depression. However, the guidelines stated morphine, or diamorphine, as the drugs of choice. The BNF did not state MI as one of the indications for pethidine. Besides, the 2 other cardiologists agreed with using morphine (MI template, pp: 384).

d- Use of iv beta-blockers and iv nitrates in acute MI patients: The guidelines recommended giving beta-blockers and nitrates intravenously if opioids fail to relieve pain. The university cardiologist stated giving these agents routinely to all acute MI patients unless there was a contraindication. The two other cardiologists, however, agreed with the guidelines (MI template, pp: 385).

e- Use of spironolactone in HF: Although it was stated in the guidelines that the use of spironolactone can not yet be recommended in mild to moderate HF. Alternatively, it was advised to reserve the drug for severe HF cases. The university and MOH cardiologists stated that using spironolactone in mild to moderate HF was a common local practice (HF template, pp: 416).
10: Templates on the Management of Chronic Stable Angina, Unstable Angina/Non-ST Segment Elevation Myocardial Infarction, Myocardial Infarction, and Heart Failure.
The School of Pharmacy
University of London

Template on the Management of Chronic Stable Angina
Locally Adopted to the Jordanian Settings

Prepared by:
Ph.D. Research Student:
Dana Darwish
Senior consultants:
Dr. Eyas Al-Mousa, Dr. Nazih Kadri and Dr. Ahmad Hassonah
Academic Supervisor:
Dr. Soraya Dhillon, Dr. Felicity Smith
**Management of Chronic Stable Angina:**

**Goals:**
1. Reduce symptoms and recurrence of ischemic episodes.
2. Prevent MI and death.

**General Measures:**
1. Smoking Cessation.
2. Life-style modification: Diet and exercise.
3. Control of hypertension.
4. Control of hyperglycaemia.

**Antianginal and Anti-ischemic Therapy:**

These include Nitrates, Beta-blockers, Calcium channel blockers and others.

**1- Beta-blockers:**

Beta-blockers are the preferred initial therapy if no contraindication (anti-ischemic therapy of choice in elderly patients) ➔ Give Beta-blockers routinely to all patients with or without prior MI in the absence of contraindications.

Cardioselective Beta-blockers, the non-selective and those with intrinsic sympathomimetic activity are equally effective.

Target heart rate is 55-60 bpm at rest (adjust dose accordingly).

If Beta-blockers are combined with Nitrates or slow-release long-acting CCB ➔ additive effect.  
(ACC/AHA, 2002)
**Dosing:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>20-80 mg twice daily</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>50-200 mg twice daily</td>
</tr>
<tr>
<td>Atenolol</td>
<td>50-200 mg/day</td>
</tr>
<tr>
<td>Nadolol</td>
<td>40-80 mg/day</td>
</tr>
<tr>
<td>Timolol</td>
<td>10 mg twice daily</td>
</tr>
<tr>
<td>Acebutolol</td>
<td>200-600 mg twice daily</td>
</tr>
<tr>
<td>Betaxolol</td>
<td>10-20 mg/day</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>10 – 20 mg/day</td>
</tr>
<tr>
<td>Esmolol (iv)</td>
<td>50-300 mcg/kg/min</td>
</tr>
<tr>
<td>Labetolol</td>
<td>200-600 mg twice daily</td>
</tr>
<tr>
<td>Pindolol</td>
<td>2.5-7.5 mg 3 times daily</td>
</tr>
</tbody>
</table>

**Contraindications:**

- **Absolute:**
  1. Severe bradycardia.
  2. High grade AV block.
  3. Sick sinus syndrome.
  4. Cardiogenic shock
  5. Severe unstable LV failure (mild CHF is an indication for b-blockers).

- **Relative:**
  1. Asthma and bronchospastic disease.
  2. Severe depression.
  3. Hypotension.
  4. Severe peripheral vascular disease with rest ischemia (CCB are preferred).

DM is not a contraindication. However, use Beta-blockers with caution in insulin-dependent diabetes.

**Side effects:**

- Fatigue
- Lethargy
- Insomnia
- Nightmares
- Impotence
- Worsening claudication

**2- Calcium Channel Blockers (CCB):**

Give long-acting or slow-release CCB as initial therapy if Beta-blockers therapy →

1. Contraindicated.
2. Leads to unacceptable side effects.
3. Unsuccessful (combine with CCB or long-acting Nitrates).
CCB and Nitrates are equivalent in long-term management of angina, however, CCB have a sustained effect (over 24 hr) without tolerance unlike the case with Nitrates.

Avoid short-acting, immediate-release Dihydropyridines in CHD.

If medical history shows features of rest and nocturnal angina (suggesting vasospasm)
→ Initiate therapy with long-acting CCB or Nitrates. (ACC/AHA, 2002)

**Dosing:**

*Dihydropyridine:*

- **Nifedipine** slow release 30-180 mg daily orally
- **Amlodipine** 5-10 mg once daily
- **Felodipine** 5-10 mg once daily
- **Isradipine** 2.5-10 mg twice daily

*Non-dihydropyridines:*

- **Verapamil**
  - Immediate release: 80-160 mg three times daily
  - Slow release: 120- 480 mg once daily. (ACC/AHA, 2002)

- **Diltiazem**
  - Immediate release: 30-60 mg 3 times daily*
  - Intermediate release: 90-120 mg twice daily*
  - Slow release: 200-300 mg once daily.* (Consensus panel)

- **Bepridil** 200 –400 mg once daily (ACC/AHA, 2002)

**Contraindications:**

1- Heart failure, except Amlodipine and Felodipine.
2- Bradycardia, sinus node dysfunction, and AV node block with Verapamil or Diltiazem. 3- Long QT interval with Bepridil.

* Doses match doses and formulations available in Jordan.
Side Effects:
Hypotension Worsening heart failure Peripheral edema Constipation
Headache Flushing Dizziness
Depression of cardiac function, bradycardia, AV dissociation, AV block and sinus node
dysfunction (with Verapamil or Diltiazem).
Polymorphic ventricular tachycardia and increased QT interval with Bepridil.

(ACC/AHA, 2002)

3- Nitroglycerine and Nitrates:

Give sublingual or spray GTN for the immediate relief of angina symptoms (up to 3 SL
tablets at 5 minute interval).

Long-term Nitrates combined with Beta-blockers or CCB ➔ Greater anti-ischemic
effect.

Isosorbide dinitrate and mononitrate are equally effective given that a sufficient nitrate-
free interval is allowed.

Use Nitrates cautiously in severe aortic stenosis.

Avoid co-administration of Sildenafil or within 24 hours of Nitrate administration.

(ACC/AHA, 2002)

Dosing:
GTN Sublingual tablets 0.3-0.6 mg up to 1.5 mg
Spray 0.4 mg as needed.
Ointment 2% 6 x 6 inch, 15 x 15 cm 7.5-40 mg
Transdermal 0.2 – 0.8 mg/h every 12 h
Oral sustained release 2.5-13 mg
Buccal 1-3 mg 3 times daily
iv 5-200 mcg/min (Tolerance in 7-8 hrs)
Isosorbide dinitrate

**Sublingual**
- 2.5 – 15 mg

**Oral**
- 5-80 mg, 2-3 times daily
- 1.25 mg daily

**Spray**
- 5 mg

**Chewable**
- 40 mg 1-2 time daily

**Oral slow release**
- 1.25 – 5 mg/h (Tolerance in 7-8 hrs)

(ACC/AHA, 2002)

Isosorbide Oral

Initially 20 mg 2-3 times daily or 40 mg twice daily

Mononitrate up to 120 mg daily in divided doses

(BNF, 2002)

**Nitrate Tolerance:** can be prevented by:
1- Less frequent administration of Nitrates with an adequate Nitrate-free interval of 8–12 hrs (most effective method).
2- Concomitant administration of Hydralazine.

**Contraindications:**
1- Hypertrophic obstructive cardiomyopathy. 2- Severe aortic valve stenosis.

**Side effects:**
1- Headache. 2- Hypotension.
3- Syncope or pre-syncope. 4- Bradycardia and hypotension with GTN (rare).

(ACC/AHA, 2002)

**4- Potassium Channel Activators:**

**Nicorandil**

Initially 10 mg twice daily (if susceptible to headache 5 mg twice daily).

Maintenance dose: 10-20 mg twice daily

Maximum dose: 30 mg twice daily.

**Contraindications:**
Cardiogenic shock   LV failure with low filling pressure   Hypotension

(BNF, 2002)
5- Other Antianginal Agents:

1- Trimetazidine, Ranolazine, and L-carnitine: Metabolic agents of anti-anginal effect in some patients.

2- Alindine and zatebradin: Bradycardic agents but their efficacy has not been yet established.

3- Sex hormones: No enough evidence to support their use.

4- Chelation therapy and acupuncture are not recommended in stable angina.

5- Antibiotics: are not recommended. (ACC/AHA, 2002)

Trimetazidine daily dose: PO 20 mg x 3. (Consensus panel)

Therapy to Prevent MI and Death:

1- Antiplatelet Agents:

Give Aspirin (75 – 325 mg) routinely every day to all patients with or without manifest symptoms in the absence of contraindications.

If Aspirin is contraindicated → Give Clopidogrel 75 mg/day (greater anti-thrombotic effect over Ticlopidine). (ACC/AHA, 2002)

Ticlopidine is given as 250 mg twice daily. (BNF, 2002)

The efficacy of GP IIb/IIIa inhibitors in stable angina is not yet established.

Avoid Dipyridamole. (ACC/AHA, 2002)

2- Angiotensin Converting Enzyme Inhibitors:

Give ACE-Inhibitors routinely to all patients with CHD, particularly high-risk patients with diabetes and/or LV systolic dysfunction, in the absence of contraindications.

**Dosing:**

Captopril 25 mg 2-3 times daily.
Up to 150 mg daily (if tolerated) in divided doses. (Amaout et al, 2003; Steffensen et al, 1995; Just et al, 1993; Akhras and Jackson, 1991)

Ramipril: Initial dose 2.5 mg once daily for 1 week, then
5 mg once daily for 3 weeks
Maintenance dose 10 mg once daily. (BNF, Sep 2002)

Lisinopril 10 mg once daily (SBP > 120 mmHg)
5 mg once daily (SBP = 100 – 120 mmHg) (BNF, Sep 2002)

Enalapril Initial dose 2.5 mg daily
Maintenance dose 20 mg/day in 1-2 divided doses. (BNF, Sep 2002)

3- Anti-thrombotic Therapy:

Low intensity anticoagulation with Warfarin in addition to Aspirin is not recommended.

Efficacy of Hirudin in stable angina is not yet established.

Clinical experience with LMWH in stable angina is still limited. (ACC/AHA, 2002)

4- Lipid-lowering Agents:

Goal LDL level is < 100 mg/dl. (NCEP/ ATP III, 2002)

For all patients obtain fasting lipoprotein profile (LDL, HDL, TG, total Cholesterol) upon admission or within 24 hours, before administration of lipid-lowering medication.

-356-
If LDL ≥ 130 mg/dl ⇒ Give LDL-lowering drugs.

If LDL level = 100-129 mg/dl ⇒ Several therapeutic options are available:
1- Start LDL-lowering therapy (advisable).

2- Postpone therapy until therapeutic measures for life-style changes are taken (weight reduction, smoking cessation, increase physical activity, dietary changes) ⇒ if <100 mg/dl could not be achieved then use drug therapy.

3- Treatment of other lipid or non-lipid risk factors: consider use of Nicotinic acid or Fibrates for elevated triglycerides or low HDL cholesterol. In addition to control of HTN and hyperglycaemia. (NCEP/ATP III, 2002; ACC/AHA, 2002)

If LDL < 100 mg/dl ⇒ LDL-lowering therapy is not required, and attention shifts to other lipids if TG > 200 mg/dl or HDL < 40 mg/dl.

Statins are the first line drugs to lower LDL (Administered with evening meal or at bed time).

If transaminases increase more than 3 times the upper limit of their normal range ⇒ Discontinue therapy. Monitor liver transaminases (ALT and AST) before and within 1-3 months of starting therapy, BNF 2002).

If Myopathy ⇒ Discontinue therapy.

Bile acid sequestrants are the second line drugs to lower LDL.
Consider Bile acid sequestrants if ⇒ 1- Moderate elevation in LDL.
2- Younger persons with elevated LDL
3- Women with elevated LDL considering pregnancy.

If TG level > 400 mg/dl ⇒ Do not give Bile acid sequestrants as mono-therapy (only when TG < 200 mg/dl).

-357-
If Bile acid sequestrants are administered ➔ Give other drugs one hour before or 4 hours after their administration.

Consider Bile acid sequestrants in combination with Statins ➔ In very high LDL-cholesterol level.

Consider Fibrates primarily in patients with high TG, high B-VLDL, low HDL and LDL near optimal.

Nicotinic acid is the most effective lipid-lowering drug for raising HDL cholesterol.

Consider Nicotinic acids in patients with low HDL, high TG, and moderately high LDL.

It is not recommended to switch from one preparation to another, because of considerable variations between different sustained-release preparations in terms of pharmacokinetics, efficacy, safety profile and adverse drug reactions.

(NCEP/ATP III, 2002; Pieper, 2003; Pieper, 2002)

Nicotinic acids can be combined with Statins ➔ Further decrease in LDL.

**Table: Lipid/lipoprotein effect of the different Lipid-lowering drugs:**

<table>
<thead>
<tr>
<th></th>
<th>Statins</th>
<th>Bile Acids</th>
<th>Nicotinic Acid</th>
<th>Fibrates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LDL</strong></td>
<td>↓18-55%</td>
<td>↑15-30%</td>
<td>↑5-25%</td>
<td>↓5-20%</td>
</tr>
<tr>
<td><strong>HDL</strong></td>
<td>↑5-15%</td>
<td>↑13-5%</td>
<td>↑15-35%</td>
<td>↑10-35%</td>
</tr>
<tr>
<td><strong>TG</strong></td>
<td>↑7-30%</td>
<td>No effect or ↑</td>
<td>↑120-50%</td>
<td>↓20-50%</td>
</tr>
</tbody>
</table>

**Doses:**

<table>
<thead>
<tr>
<th></th>
<th>Initial dose</th>
<th>Maximum FDA-approved dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20 mg</td>
<td>80 mg (Max 10 mg daily with concomitant Ciclosporin, Fibrates, or lipid-lowering dose of Nicotinic acid; BNF, 2002)</td>
</tr>
<tr>
<td>Drug</td>
<td>Dose</td>
<td>Dose</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------</td>
<td>--------</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20 mg (40mg)</td>
<td>80 mg</td>
</tr>
<tr>
<td>Atrovastatin</td>
<td>10 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Fibrates:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>600 mg twice/day</td>
<td>1200 mg</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>200 mg once daily</td>
<td>200 mg</td>
</tr>
<tr>
<td>Clofibrate</td>
<td>1000 mg twice/day</td>
<td>2000 mg</td>
</tr>
<tr>
<td>Bile acid sequestrants:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>4-16 g</td>
<td>24 g</td>
</tr>
<tr>
<td>Colestipol</td>
<td>5- 20 g</td>
<td>30 g</td>
</tr>
<tr>
<td>Colesevelam</td>
<td>2.6- 3.8 g</td>
<td>4.4 g</td>
</tr>
<tr>
<td>Nicotinic Acid:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystalline</td>
<td>1.5-3 g</td>
<td>4.5 g</td>
</tr>
<tr>
<td>Sustained-release</td>
<td>1-2 g</td>
<td>2 g</td>
</tr>
<tr>
<td>Extended release</td>
<td>2 g</td>
<td>2 g</td>
</tr>
<tr>
<td>Contraindications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins: Absolute:</td>
<td>Active or chronic liver disease.</td>
<td></td>
</tr>
<tr>
<td>Relative: concomitant use of Ciclosporin, macrolide antibiotics, antifungal agents and Cytochrome P-450 inhibitors (Fibrates and Nicotinic acid should be used with caution).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrates: Severe hepatic or renal insufficiency.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile acid sequestrants: Absolute: Familial dysbeta-lipoproteinemia, TG &gt; 400 mg/dl.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative: TG &gt;200 mg/dl.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid: Absolute: Chronic liver disease, severe gout.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative: hyperuricemia, high doses in DM type II. (NCEP/ATP III, 2002)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Side Effects:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins: Myopathy and increased liver transaminases.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrates: Dyspepsia, various upper GI complaints, cholesterol gallstones, and myopathy.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bile acid sequestrants: Upper and lower gastrointestinal complaints, decreased absorption of other drugs.

Nicotinic acid: Flushing, hyperglycaemia, hyperuricemia or gout, upper GI distress, hepato-toxicity, especially with sustained-release form. (NCEP/ATP III, 2002)

Summary:
Give Aspirin, Beta-blockers, and lipid-lowering drugs to all patients in the absence of contraindications.
Give ACE-Inhibitors to all patients particularly diabetics and/or LVSD.
If Beta-blockers use Contraindicated, leads to unacceptable side effects, or inadequate or unsuccessful → Give long-acting or slow-release CCB.
If CCB use Contraindicated, leads to unacceptable side effects, or ineffective → Give long-acting Nitrates.

Follow-up on Patients:
1- Relief of ischemic pain.
2- Blood pressure and control of hypertension.
3- Blood glucose level and control of hyperglycaemia.
4- Lipid profile, particularly LDL-cholesterol level.
Table: Recommended anti-anginal drug therapy (CCB vs Beta-blockers) in angina associated with other conditions (source ACC/AHA, 2002):

<table>
<thead>
<tr>
<th>Condition Concomitant to Stable Angina</th>
<th>Recommended Drug</th>
<th>Avoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic hypertension</td>
<td>Beta-blockers (CCB)</td>
<td></td>
</tr>
<tr>
<td>Migraine or vascular headache</td>
<td>Beta-blockers (Verapamil or Diltiazem)</td>
<td></td>
</tr>
<tr>
<td>Asthma or COPD with bronchospasm</td>
<td>Verapamil or Diltiazem</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Beta-blockers</td>
<td></td>
</tr>
<tr>
<td>Raynaud’s syndrome</td>
<td>Long-acting slow-release CCB</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Insulin-dependent DM</td>
<td>Beta-blockers (particularly if prior MI) or long-acting slow-release CCB</td>
<td></td>
</tr>
<tr>
<td>Non-insulin dependent DM</td>
<td>Beta-blockers or long-acting slow-release CCB</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>Long-acting slow-release CCB</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Mild peripheral vascular disease</td>
<td>Beta-blockers or CCB</td>
<td></td>
</tr>
<tr>
<td>Severe peripheral vascular disease with rest ischemia</td>
<td>CCB</td>
<td>Beta-blockers</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td>Long-acting slow-release CCB (dihydropyridines)</td>
<td>Beta-blockers, Verapamil, Diltiazem</td>
</tr>
<tr>
<td>Sinus tachycardia (not due to heart failure)</td>
<td>Beta-blockers</td>
<td></td>
</tr>
<tr>
<td>Supraventricular Tachycardia</td>
<td>Verapamil, Diltiazem or Beta-blockers</td>
<td></td>
</tr>
<tr>
<td>AV block</td>
<td>Long-acting slow-release CCB (dihydropyridines)</td>
<td>Beta-blockers, Verapamil, Diltiazem</td>
</tr>
<tr>
<td>Rapid atrial fibrillation (with digitalis)</td>
<td>Verapamil, Diltiazem, or Beta-blockers</td>
<td></td>
</tr>
<tr>
<td>Ventricular Arrhythmias</td>
<td>Beta-blockers</td>
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</tr>
<tr>
<td>CHF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (LVEF &gt; 40%)</td>
<td>Beta-blockers</td>
<td>Verapamil, Diltiazem</td>
</tr>
<tr>
<td>Moderate to Severe (LVEF &lt; 40%)</td>
<td>Amlodipine or Felodipine (Nitrates)</td>
<td></td>
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<tr>
<td>Mild aortic stenosis</td>
<td>Beta-blockers</td>
<td></td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>Long-acting slow-release Dihydropyridines</td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>Long-acting slow-release dihydropyridines</td>
<td></td>
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<tr>
<td>Mitral stenosis</td>
<td>Beta-blockers</td>
<td></td>
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<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>Beta-blockers, non-dihydropyridine CCB</td>
<td>Nitrates, Dihydropyridines</td>
</tr>
</tbody>
</table>
References:


8- Levy S and the Group of South of France Investigators. **Combination Therapy of Trimetazidine with Diltiazem in Patients with Coronary Artery Disease.** Am J Cardiol 1995, 76: 12B-16B.

9- Manchanda SC. **Treatment of Stable Angina With Low Dose Diltiazem in Combination With the Metabolic Agent Trimetazidine.** Int J Cardiol. 2003 Mar; 88 (1): 83-9.


Template on the Management of Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction
Locally Adopted to the Jordanian Settings

Prepared by:

Ph.D. Research Student: Dana Darwish
Senior consultants: Dr. Eyas Al-Mousa, Dr. Nazih Kadri and Dr. Ahmad Hassonah
Academic Supervisor: Dr. Soraya Dhillon, Dr. Felicity Smith
Goals of Management:
1. Relief of signs and symptoms of ischemia.
2. Prevention of serious adverse outcomes (death, MI/re-infarction).

General Measures:
Treatment of major risk factors:
1. Smoking cessation.
2. Control of hyperglycaemia in DM.

Management Measures:
1. Anti-ischemic therapy.
2. Antiplatelet and anticoagulant therapy.
3. Ongoing risk stratification.
4. Use of invasive procedures.
5. Treatment of underlying disease process (hypertension, anaemia, hyperthyroidism, arrhythmias, and heart failure).

This template will only discuss medical therapy for UA/NSTEMI. Recommendations regarding invasive procedures are beyond the scope of this template.

Anti-Ischemic Therapy:
It includes: Nitrates, Morphine sulfate, Beta-blockers, Calcium channel blockers (CCB), ACE-Inhibitors, Potassium channel activators.

1- Nitrates:
Give GTN sublingually 0.3-0.6 mg (up to 1.5 mg) or spray (0.4 mg), dose can be repeated up to 3 doses at 5 minutes interval in the absence of contraindications. This is followed by oral or topical Nitrate if no ongoing ischemic symptoms.

Give iv Nitrates if → 1- Ongoing ischemic symptoms are not relieved with SL GTN and iv Beta-blockers.
2 - All non-hypotensive, high-risk patients.
Use GTN with caution if → SBP < 110 mmHg in normotensive patients.

SBP decreased by more than 25% below starting SBP reading in hypertensive patients.

If GTN continuous iv infusion → Increase infusion rate periodically to maintain is required more than 24 hours efficacy.

If patient is pain free and no signs or symptoms of ischemia for 12-24 hours → Decrease dose of iv GTN and switch to oral or topical Nitrates.

Avoid abrupt cessation of Nitrates (Decrease dose gradually). (ACC/AHA, 2002)

**Dosing:**

GTN Continuous infusion → Initially 5-10 mcg/min, then increased by 10 mcg/min every 3-5 minutes until some response of symptom (observe blood pressure). If no response is seen → increase increments by 20 mcg/min.

Maximum dose: A ceiling of 200 mcg/min is commonly used.

Topical 0.2-0.8 mg/hr every 12 hours (= 5 – 10 mg patch/ 24 hours)

If signs and symptoms are relieved → Stop increasing dose.

If not relieved → Continue increasing dose until a blood pressure response is observed, then reduce dose increase and lengthen intervals between increments.

Isosorbide dinitrate SL 5-10 mg (BNF, 2002)

oral 5-80 mg 2-3 times daily

Slow release: 40 mg 1-2 times daily (ACC/AHA, 2002)

iv infusion: 2-10 mg/hr, higher doses up to 20 mg/hr may be required. (BNF, 2002)

Isosorbide mononitrate oral 20 mg twice daily

Slow release 60-240 mg once daily

Side effects: Headache, hypotension and tolerance. (ACC/AHA, 2002)
2- Morphine sulfate:
Give morphine sulfate (1-5 mg iv) if 1- Symptoms not relieved after 3 serial SL GTN
2- Acute pulmonary congestion
and/or 3- Severe agitation, pain or anxiety is present.
Repeat dose every 5-30 minutes as needed (to relieve symptoms and maintain patient comfort). (ACC/AHA, 2002)

Give concomitant anti-emetic (Metoclopramide 10 mg iv injection, or Cyclizine 50 mg iv injection (if LV function is not compromised). (BNF, 2002)

If morphine overdose ➔ Give Naloxone (0.4-2 mg iv).

If administered with iv GTN ➔ Monitor blood pressure carefully.

Do not give morphine sulfate if patient is hypotensive.

If allergy to morphine ➔ Give Meperidine HCl. (ACC/AHA, 2002)

Side effects:
1- Hypotension especially in volume depletion and/or vasodilator therapy ➔ Give:
   a- iv saline boluses.  b- Atropine if accompanied with bradycardia.
2- Nausea and vomiting.
3- Respiratory depression. (ACC/AHA, 2002)

3- Beta-blockers:
Give Beta-blockers routinely early in the management of UA/NSTEMI if no contraindications.
Give the first dose iv, followed by oral administration ➔ if ongoing chest pain or high risk patients.
Give Beta-blockers orally if ➔ Low or intermediate risk patients.

Initial choice agents include Propranolol, Metoprolol and Atenolol. There is no evidence that any member of this class is more effective than another.
Choice of Beta-blocker is based on pharmacokinetics, side effects and physician’s familiarity. (ACC/AHA, 2002)

Beta-blockers with intrinsic sympathomimetic activity are not preferred (Acebutolol, Labetalol, Pindolol).

If ultra-short acting agent is required ➔ Give Esmolol.

Delay initiation of Beta-blockers if ➔
1- Significant bradycardia HR < 50 bpm.
2- Hypotension: SBP < 90 mmHg.

Give with caution a low dose of short-acting Beta1-selective agent (2.5 mg Metoprolol iv, or 12.5 mg Metoprolol orally or 25 mcg/kg/min Esmolol iv) if ➔

1- Significant COPD with component of reactive airway disease.
2- Mild wheezing or history of COPD.
3- Concern about Beta-blocker intolerance. (ACC/AHA, 2002)

Contraindications:
1- Marked first degree AV block.
2- Any form of second or third degree AV block in the absence of a functioning pacemaker.
3- Sick sinus syndrome. 4- Cardiogenic shock. 5- Hypotension.
6- Severe LVSD in CHF (should not receive Beta-blockers on acute basis).
7- History of asthma and bronchospastic element. (ACC/AHA, 2002)

DM is not a contraindication. (BNF, 2002)

Use Beta-blocker with caution in insulin dependent DM patients, and those with frequent hypoglycaemic attacks (COMET trial ➔ Carvedilol increases insulin sensitivity).

Dosing:
Metoprolol: Initially 5 mg iv slowly (over 1-2 minutes), repeated every 5 minutes at 5 mg increments for a total initial dose of 15 mg. If tolerated ➔ Initiate oral Metoprolol 15
minutes after last iv dose at 25-50 mg every 6 hours for 48 hours → Maintain at 100 mg twice daily. (ACC/AHA, 2002)

**Propranolol**: Initially 0.5-1 mg iv, followed in 1-2 hours by 40-80 mg orally 2-3 times daily.

**Esmolol**: Initially 0.1 mg/kg/min with titration every 10-15 minutes in increments of 0.05 g/kg/min according to blood pressure response, until:
1- Desired response has been achieved.
2- Limiting symptoms develop.
3- A dosage of 0.3 mg/kg/min is reached.
If a more rapid onset of action is desired → give loading dose of 0.5 mg/kg by slow iv administration (over 2-5 minutes). (ACC/AHA, 2002)

**Atenolol**: Initially 5 mg iv repeated after five minutes. Then after 1-20 hours from iv dose give 50-100 mg/day orally.

During iv Beta-blocker administration → Monitor: 1- heart rate. 2- blood pressure. 3- ECG. 4- Auscultation of rales and bronchospasm.

Target resting heart rate is 50-60 bpm unless a limiting side effect occurs. (ACC/AHA, 2002)

Patients without limiting side effects during iv administration are to be converted to oral regimens. Maintenance doses are as follows:

- **Propranolol**: 20-80 mg twice daily
- **Metoprolol**: 50-200 mg twice daily
- **Atenolol**: 50-200 mg/day
- **Nadolol**: 40-80 mg/day
- **Timolol**: 10 mg twice daily
- **Acebutolol**: 200-600 mg twice daily
- **Betaxolol**: 10-20 mg/day (ACC/AHA, 2002)
4- Calcium Channel Blockers (CCB):

Reserve CCB as second or third choice after initiation of Nitrates or Beta-blockers.

Verapamil and Diltiazem are the preferred agents.

Avoid short-acting, immediate-release Dihydropyridines in CHD patients.

Give Verapamil or Diltiazem as initial therapy if Beta-blockers are contraindicated or ischemia is continuing or frequently recurring in the absence of contraindications and severe LVSD.

Add CCB to therapy if → Ongoing or recurring ischemic symptoms in:
1- Patients already receiving adequate doses of Nitrates and Beta-blockers.
2- Patients unable to tolerate adequate doses of Nitrates and/or Beta-blockers.
3- Management of HTN in patients with recurrent UA.

Dosing:

Dihydropyridine:
Nifedipine  slow release 30-180 mg daily orally
Amlodipine  5-10 mg once daily (Long acting)
Felodipine  5-10 mg once daily (Long acting)
Isradipine  2.5-10 mg twice daily

Non-dihydropyridines:
Verapamil  Immediate release: 80-160 mg three times daily
          Slow release: 120-480 mg once daily.  (ACC/AHA, 2002)
Diltiazem  Immediate release: 30-60 mg 3 times daily*
  Intermediate release: 90-120 mg twice daily.*
  Slow release: 200-300 mg once daily.*  (Consensus Panel)

Bepridil  200 –400 mg once daily.  (ACC/AHA, 2002)

* Doses match doses and formulations available in Jordan.

**Contraindications:**
1- Heart failure, except Amlodipine and Felodipine.
2- Bradycardia, sinus node syndrome, and AV nodal block with Verapamil and Diltiazem.
3- Long QT interval with Bepridil.  (ACC/AHA, 2002)

**Side effects:**
Hypotension  Worsening CHF  Bradycardia  AV block.  (ACC/AHA, 2002)

**5- ACE-Inhibitors:**
Give ACE-Inhibitors to all UA/NSTEMI patients, particularly:
1- Recent MI.
2- High risk chronic CHD, with or without LVSD.
3- DM.
4- LVSD or CHF.
5- Hypertension not controlled by Beta-blockers and Nitrates.  (ACC/AHA, 2002)

**Dosing:**
Captopril  Initial dose 6.25 mg, increased over several weeks up to 150 mg daily (if tolerated) in divided doses.

Ramipril  Initial dose  2.5 mg once daily for 1 week, then 5 mg once daily for 3 weeks
  Maintenance dose  10 mg once daily.

Lisinopril 10 mg x 1 (SBP >120 mmHg)
  5 mg x 1 (SBP = 100-120 mmHg)
Enalapril

Initial dose 2.5 mg daily
Maintenance dose 20 mg/day in 1-2 divided doses. (BNF, 2002)

6- Potassium Channel Activator:
Nicorandil Add to conventional treatment significant reduction in transient myocardial infarction, ventricular and supra-ventricular tachycardia. (ACC/AHA, 2002)

Dosing:
Initially 10 mg twice daily (if susceptible to headache 5 mg twice daily)
Maintenance dose: 10-20 mg twice daily
Maximum dose: 30 mg twice daily.

Contraindications:
Cardiogenic shock LV failure with low filling pressure Hypotension (BNF, 2002)

7- Antiplatelet and Anticoagulation Therapy:
These include:
1- Oral antiplatelet therapy: e.g. Aspirin, Clopidogrel, Ticlopidine.
2- Anticoagulants: Heparin, LMWH (Dalteparin, Enoxaparin, Tinzaparin), Hirudin, Warfarin.
3- Intravenous Antiplatelet therapy (GP IIb/IIIa antagonists): Abciximab, Eptifibatide, Tirofiban. (ACC/AHA, 2002)

7.1- Oral Antiplatelet Therapy:
Initiate ASA as soon as possible after diagnosis of UA/NSTEMI and continue indefinitely, unless contraindications develop.

If ASA could not be administered due to Give Clopidogrel (preferable) or Ticlopidine hypersensitivity or major gastrointestinal contraindication(primarily recent bleeding from peptic ulcer or gastritis).

In acute situations give a loading dose of Clopidogrel at 300 mg to achieve more rapid platelet inhibition.
Add Clopidogrel to ASA as soon as possible on admission and continue for at least 1 month and up to 9 months if 1- Early non-interventional approach is planned.
  or 2- Percutaneous coronary intervention (PCI) is planned and no high risk for bleeding.

Do not start Clopidogrel until it is clear that CABG will not be scheduled within the next several days.

Withhold Clopidogrel at least 5-7 days before CABG or surgery.

Give Heparin or LMWH with Clopidogrel or Ticlopidine.  (ACC/AHA, 2002)

**Dosing:**

**Aspirin:**
- Initial dose: 160-325 mg (non-enteric formulation)
- Maintenance dose: 75-160 mg/day

**Clopidogrel:** 75 mg/day.
- Loading dose of 300-600 mg can be used if rapid onset of action is required.
- CURE trial ➔ Favorable results with 9 months duration of therapy.

**Ticlopidine:** 250 mg twice daily.
- Loading dose of 500 mg can be used when rapid onset is required; monitoring of platelet and white cell counts during treatment is required.
  (ACC/AHA, 2002)

**Side effects:**

**Ticlopidine:**
1- GI problems: Nausea, vomiting, abdominal pain, diarrhoea.
2- Neutropenia: resolves within 1-3 weeks of discontinuing therapy, very rare may be fatal). Severe cases in 0.8% of patients.
3- Thrombotic Thrombocytopenia Purpura (TTP): rare and requires immediate plasma exchange.
Complete blood count, which includes a differential count every 2 weeks for the first three months of therapy.


(ACC/AHA, 2002)

Contraindications to Oral Antiplatelet Therapy:
1- Aspirin: intolerance - allergy (primarily manifested as allergy) – active bleeding –
hemophilia – active retinal bleeding – severe untreated hypertension – active peptic ulcer or other serious sources of GI or genitourinary bleeding. (ACC/AHA, 2002)

Drug Interactions:
There is a negative interaction between ASA and ACE-Inhibitors, however it does not seem to interfere with the clinical benefits of therapy with either agent. (ACC/AHA, 2002)

7.2- Anticoagulant Therapy:
Give subcutaneous LMWH or iv Heparin with ASA and/or Clopidogrel.
Enoxaparin is preferable to Heparin in UA/NSTEMI, unless CABG is planned within 24 hours
(FRIC trial → Dalteparin showed unfavorable trends towards worse therapy outcome over Heparin in UA/NSTEMI, FRAXIS trial → more frequent death or MI with Nadroparin over Heparin).

Heparin is preferred over LMWH in CABG.

LMWH can be given safely to patients undergoing PCI (NICE-1 trial, Enoxaparin 1mg/kg). Alternatively, give LMWH during initial stabilization of patients, withhold dose on the morning of PCI, and if more than 8 hours elapsed since last dose of LMWH, give Heparin for PCI.

Avoid abrupt cessation of Heparin → switch from iv to SC for several days before withdrawal.
Give Hirudin if Heparin-induced thrombocytopenia.

Low or moderate-intensity anticoagulation with fixed dose Warfarin is not recommended for routine use after hospitalization in UA/NSTEMI.

Give Warfarin to UA/NSTEMI patients with established indications such as atrial fibrillation or mechanical prosthetic heart valves. (ACC/AHA, 2002)

**Dosing of Anticoagulant Therapy:**

**Heparin:** Weight adjusted regimen.

- iv bolus 60-70 U/kg (maximum 5000 U) followed by Infusion: 12-15 U/kg/hr (maximum 1000 U/hr), titrated to aPTT 1.5-2.5 times control.
- Monitoring aPTT to achieve values 1.5-2.5 times control (adjust dose accordingly).
- Measurements should be made 6 hours after any dosage change and used to adjust Heparin infusion until the aPTT exhibits a therapeutic level.
- When 2 consecutive aPTT values are therapeutic perform measurement every 24 hours.
- aPTT should be promptly measured with significant change in the patient’s clinical condition: 1- recurrent ischemia, 2- bleeding, 3- hypotension. Followed by dose adjustment if necessary.
- Serial hemoglobin/ hematocrit and platelet measurements are recommended at least daily during Heparin therapy.
- If hemodynamic instability, recurrent symptoms, or significant bleeding, immediately determine hemoglobin/hematocrit.
- Duration of therapy: Most trials continued therapy for 2-5 days.

**Dalteparin:** 120 IU/kg SC every 12 hr (maximum 10,000 IU twice daily).

**Enoxaparin:** 1 mg/kg SC every 12 hr.

A bolus dose of 30 mg iv could be given before the first dose.
Hirudin: 0.4 mg/kg iv bolus over 15 to 20 seconds, followed by continuous iv infusion of 0.15 mg/kg/hr. Adjust infusion to a target range of 1.5-2.5 times the control aPTT values. (ACC/AHA, 2002)

**Side effects:**

Heparin:

1- Heparin-induced thrombocytopenia (monitored by serial platelet counts).
2- Auto-immune Heparin-induced thrombocytopenia with thrombosis (dangerous but rare) ⇒ immediate cessation of all Heparin therapy (including Heparin used to flush iv lines). (ACC/AHA, 2002)

### 7.3- Intravenous Antiplatelet Therapy:

GP IIb/IIIa antagonists ⇒ Substantial benefit in UA/NSTEMI patients undergoing PCI.
Questionable benefit in patients who do not undergo PCI.

Give Platelet GP IIb/IIIa antagonist in addition to:

1- ASA, Heparin and/or Clopidogrel if ⇒ Catheterization and PCI are planned. They may be administered just prior to PCI.

2- ASA and Heparin or LMWH if ⇒ Continuing ischemia, elevated troponin or with high-risk features in whom an invasive management strategy is not planned.

Intensity of therapy should be tailored to individual risk.

Abciximab is approved for treatment of UA/NSTEMI as an adjunct to PCI or when PCI is planned within 24 hr.

Tirofiban and Eptifibatide are approved for treatment of UA/NSTEMI who are managed medically or with PCI, in combination with ASA and Heparin (Do not use Tirofiban alone in UA patients).

Tirofiban or Eptifibatide are more optimal than Abciximab in patients likely to need CABG.

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When GP IIb/IIIa antagonists are given concurrently with Heparin ➔ Decrease dose of Heparin below recommended to achieve best outcome in PCI setting.

GP IIb/IIIa antagonists can be used with LMWH. Combination is not associated with excess bleeding whether or not PCI was performed. (ACC/AHA, 2002)

**Dosing:**

Abciximab: 0.25 mg/kg bolus followed by infusion of 0.125 mcg/kg/min (Maximum 10 mcg/min) for 12 to 24 hr.

Eptifibatide: 180 mcg/kg bolus, followed by infusion of 2 mcg/kg/min for 72 to 96 hr

Tirofiban: 0.4 mcg/kg/min for 30 minutes, followed by Infusion of 0.1 mcg/kg/min for 48 to 96 hr. (ACC/AHA, 2002)

**Side effects with GP IIb/IIIa antagonists:**

1- Increase risk of bleeding.
2- Thrombocytopenia: unusual and reversible. (ACC/AHA, 2002)

**Monitoring GP IIb/IIIa antagonists:**

Monitor haemoglobin, platelet count and bleeding signs on daily basis during administration of drugs.

8- **Lipid-lowering Agents:**

Goal LDL level is < 100 mg/dl. (NCEP/ ATP III, 2002)

For all patients obtain fasting lipoprotein profile (LDL, HDL, TG, total Cholesterol) upon admission or within 24 hours, before administration of lipid-lowering medication.

If LDL ≥ 130 mg/dl ➔ Give LDL-lowering drugs.

ATP III classification of LDL, HDL and total cholesterol:

<table>
<thead>
<tr>
<th>LDL level (mg/dl)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>Optimal</td>
</tr>
<tr>
<td>100-129</td>
<td>Near or above optimal</td>
</tr>
<tr>
<td>130-159</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160-189</td>
<td>High</td>
</tr>
<tr>
<td>≥ 190</td>
<td>very high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total cholesterol level (mg/dl)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 200</td>
<td>Desirable</td>
</tr>
<tr>
<td>200-239</td>
<td>Borderline high</td>
</tr>
<tr>
<td>≥ 240</td>
<td>High</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HDL level (mg/dl)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>low</td>
</tr>
<tr>
<td>≥ 60</td>
<td>high</td>
</tr>
</tbody>
</table>
If LDL level = 100-129 mg/dl ➔ Several therapeutic options are available:

1- Start LDL- therapy (advisable).
2- Postpone therapy until therapeutic life-style changes measures are taken (weight reduction, smoking cessation, increase physical activity, dietary changes) ➔ if <100 mg/dl could not be achieved then use drug therapy.
3- Treatment of other lipid or non-lipid risk factors: consider use of Nicotinic acid or Fibrates for elevated triglycerides or low HDL cholesterol. In addition to control of HTN and hyperglycemia. (NCEP/ATP III, 2002; ACC/AHA, 2002)

If LDL < 100 mg/dl ➔ LDL-lowering therapy is not required, and attention shifts to other lipids if TG > 200 mg/dl or HDL < 40 mg/dl.

Statins are the first line drugs to lower LDL (Administered with evening meal or at bed time).

If transaminases increase more than 3 times the upper limit of their normal range ➔ Discontinue therapy. Monitor liver transaminases (ALT and AST) before and within 1-3 months of starting therapy, BNF 2002).

If Myopathy ➔ Discontinue therapy.

Bile acid sequestrants are the second line drugs to lower LDL. Consider them if:

1- Moderate elevation in LDL.
2- Younger persons with elevated LDL
3- Women with elevated LDL considering pregnancy.

If TG level > 400 mg/dl ➔ Do not give Bile acid sequestrants as mono-therapy (only when TG < 200 mg/dl).

If Bile acid sequestrants are administered ➔ Give other drugs one hour before or 4 hours after their administration.
Consider Bile acid sequestrants in combination with Statins in very high LDL-cholesterol level.

Consider Fibrates primarily in patients with high TG, high B-VLDL, low HDL and LDL near optimal.

Nicotinic acid is the most effective lipid-lowering drug for raising HDL cholesterol.

Consider Nicotinic acids in patients with low HDL, high TG, and moderately high LDL.

It is not recommended to switch from one preparation to another, because of considerable variations between different sustained-release preparations in terms of pharmacokinetics, efficacy, safety profile and adverse drug reactions.

(NCEP/ATP III, 2002; Pieper, 2003; Pieper, 2002)

Nicotinic acids can be combined with Statins Further decrease in LDL.

Table: Lipid/lipoprotein effect of the different Lipid-lowering drugs:

<table>
<thead>
<tr>
<th></th>
<th>Statins</th>
<th>Bile Acids</th>
<th>Nicotinic Acid</th>
<th>Fibrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL</td>
<td>118-55%</td>
<td>115-30%</td>
<td>15-25%</td>
<td>15-20%</td>
</tr>
<tr>
<td>HDL</td>
<td>5-15%</td>
<td>3-5%</td>
<td>15-35%</td>
<td>10-35%</td>
</tr>
<tr>
<td>TG</td>
<td>17-30%</td>
<td>No effect or</td>
<td>120-50%</td>
<td>120-50%</td>
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Doses:

<table>
<thead>
<tr>
<th>Statins:</th>
<th>Initial dose</th>
<th>Maximum FDA-approved dose</th>
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</thead>
<tbody>
<tr>
<td>Lovastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20 mg</td>
<td>80 mg (Max 10 mg daily with concomitant Ciclosporin, Fibrates, or lipid-lowering dose of Nicotinic acid; BNF, 2002)</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20 mg (40mg)</td>
<td>80 mg</td>
</tr>
<tr>
<td>Atrovastatin</td>
<td>10 mg</td>
<td>80 mg (NCEP/ATP III, 2002)</td>
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Fibrates:  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual daily dose</th>
<th>Maximum dose</th>
</tr>
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<tbody>
<tr>
<td>Gemfibrozil</td>
<td>600 mg twice/day</td>
<td>1200 mg</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>200 mg once daily</td>
<td>200 mg</td>
</tr>
<tr>
<td>Clofibrate</td>
<td>1000 mg twice/day</td>
<td>2000 mg</td>
</tr>
</tbody>
</table>

*NCEP/ATP III, 2002*

Bile acid sequestrants:  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual daily dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholestyramine</td>
<td>4-16 g</td>
<td>24 g</td>
</tr>
<tr>
<td>Colestipol</td>
<td>5-20 g</td>
<td>30 g</td>
</tr>
<tr>
<td>Colesevelam</td>
<td>2.6-3.8g</td>
<td>4.4 g</td>
</tr>
</tbody>
</table>

*NCEP/ATP III, 2002*

Nicotinic Acid:  

<table>
<thead>
<tr>
<th>Form</th>
<th>Usual daily dose</th>
<th>Maximum dose</th>
</tr>
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<tbody>
<tr>
<td>Crystalline</td>
<td>1.5-3 g</td>
<td>4.5 g</td>
</tr>
<tr>
<td>Sustained-release</td>
<td>1-2 g</td>
<td>2 g</td>
</tr>
<tr>
<td>Extended release</td>
<td>2 g</td>
<td>2 g</td>
</tr>
</tbody>
</table>

*NCEP/ATP III, 2002*

Contraindications:

**Statins:**  
Absolute: Active or chronic liver disease.
Relative: concomitant use of ciclosporin, macrolide antibiotics, antifungal agents and cytochrome P-450 inhibitors (Fibrates and Nicotinic acid should be used with caution).

**Fibrates:** Severe hepatic or renal insufficiency.

**Bile acid sequestrants:** Absolute: Familial dysbeta-lipoproteinemia, TG > 400 mg/dl.
Relative: TG >200 mg/dl.

**Nicotinic Acid:**  
Absolute: Chronic liver disease, severe gout.
Relative: hyperuricemia, high doses in DM type II.  

*NCEP/ATP III, 2002*

**Major Side Effects:**  
**Statins:** Myopathy and increased liver transaminases.
**Fibrates:** Dyspepsia, various upper GI complaints, cholesterol gallstones, and myopathy.
Bile acid sequestrants: Upper and lower gastrointestinal complaints, decreased absorption of other drugs.

Nicotinic acid: Flushing, hyperglycemia, hyperuricemia or gout, upper GI distress, hepato-toxicity, especially with sustained-release form.

(NCEP/ATP III, 2002)

Prescribing Practice for which Conflicting Evidence Exists, which is not in Favour of Practice:
1- Extended-release non-dihydropyridine CCB (Verapamil and Diltiazem) instead of Beta-blockers.
2- Immediate-release Dihydropyridine CCB (Nifedipine) in the presence of Beta-blockers.
3- Eptifibatide or Tirofiban in addition to ASA and LMWH or UFH to patients without continuing ischemia, who have no other high-risk features and in whom PCI is not planned. (ACC/AHA, 2002)

Not Recommended Practice:
- GTN or other Nitrates within 24 hours of Sildenafil administration (Viagra).
- Immediate-release, short-acting Dihydropyridine CCB (e.g. Nifedipine) in the absence of concurrent adequate Beta-blockers.
- Verapamil and Diltiazem in pulmonary edema or severe LV dysfunction.
- Thrombolytic therapy.
- Abciximab administration if PCI is not planned.
- Sulfinpyrazone, Dipyridamole, Prostacyclin or Prostacyclin analogue (have no benefit in UA/NSTEMI). (ACC/AHA, 2002)

Discharge Medication:
UA/NSTEMI patients should receive GTN on PRN basis, a Beta-blocker orally, ACE-Inhibitor to control HTN, LVD or post MI, GTN on PRN basis, along with Antiplatelet therapy, as well as Lipid-lowering therapy (depending on LDL level). (ACC/AHA, 2002)
References:


Template on the Management of Myocardial Infarction
Locally Adopted to the Jordanian Settings

Prepared by:
Ph.D. Research Student: Dana Darwish
Senior consultants: Dr. Eys Al-Mousa, Dr. Nazih Kadri and Dr. Ahmad Hassonah
Academic Supervisor: Dr. Soraya Dhillon, Dr. Felicity Smith
These guidelines do not override or replace health care professional’s clinical judgement, experience and common sense to make appropriate decisions in light of patient’s circumstances.

Recommendations in these guidelines pertain to MI patients presenting with ischemic symptoms and persistent ST-segment elevation on ECG.

**Emergency and Early in-Hospital Care:**

**Goals:**

1. Relieve pain.
2. Prevent or treat cardiac arrest.
3. Initiate reperfusion therapy as soon as possible.
4. Treat immediate complications such as pump failure, shock and life-threatening arrhythmia.

**1- Relief of Pain, Breathlessness and Anxiety:**

**1.1- Opioids:**

Give intravenous opioids (morphine or Diamorphine) until pain is relieved.
Morphine: slow iv injection 4-8 mg with additional doses of 2 mg at 5 min intervals until pain is relieved. Reduce dose by half in elderly or frail patients. Avoid IM injection.  
(ESC, 2003; BNF, 2002)

Diamorphine: 5 mg slow iv injection (1 mg/min), followed by further 2.5-5 mg if needed (reduce dose by half in frail or elderly).  
(BNF, 2002)

Give concurrently antiemetic therapy: Metoclopramide 10 mg iv injection, or Cyclizine 50 mg iv injection (if left ventricular function is not compromised).  
(BNF, 2002)

If hypotension and bradycardia occur ➔ Give Atropine.  
(ESC, 2003)

Atropine dose: 0.3-1 mg iv, can be repeated if necessary.  
(BNF, 2002)

If respiratory depression ➔ Give Naloxone.  
(ESC, 2003)
Naloxone dose: 100-200 mcg (1.5-3 mcg/kg), if necessary additional doses of 100 mcg every 2 minutes.  

(BNF, 2002)

If opioids fail to relieve pain on repeated administration ➔ Give iv Beta-blockers or Nitrates.  

(ESC, 2002)

If anxiety and patient is excessively disturbed ➔ Tranquilizers may be helpful.

If cardiac arrest ➔ Advanced life support, alternatively, if not available basic life support.

2- Reperfusion Therapy to Restore Myocardial Tissue Perfusion:

Give reperfusion therapy to all MI patients with history of chest pain <12 hr.

2.1- Primary PCI:

This is the preferred treatment if performed < 90 min after first medical contact.

If patient is in shock or fibrinolytic therapy is contraindicated ➔ Perform PCI.

Give Abciximab in primary PCI, with or without stenting, along with a low-dose Heparin.  

(ESC, 2003)

2.2- Fibrinolytic Treatment:

Give Aspirin concomitantly with fibrinolytic therapy in all patients unless contraindicated.

If patient did not receive Aspirin ➔ Give 150-325 mg chewable or dispensed in water (not enteric coated).

If oral ingestion is not possible ➔ Give iv Aspirin 250 mg.  

(ESC, 2003)

If Aspirin is contraindicated ➔ Give Clopidogrel or Ticlopidine.  

(ACC/AHA, 1999)

Initiate fibrinolytic therapy as soon as possible if ➔ No contraindications and primary PCI can not be performed.

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Do not wait for lab results on MI markers (CK-MB, troponin) to initiate reperfusion therapy.

Initiate fibrinolytic therapy within <12 hrs of onset of symptoms.

If more than 12 hrs elapse after establishing MI → Do not give fibrinolytic therapy unless evidence for ongoing ischemia exists.

In patients presenting late (> 4hr after symptom onset) → Alteplase or tenecteplase are preferred.

Accelerated t-PA (over 90 min) with aPTT adjusted iv Heparin is associated with lower death rate and higher risk of stroke than streptokinase or Anistreplase.

Double bolus Reteplase (r-PA) has no advantage over t-PA except easier administration.

Single bolus weight-adjusted tenecteplase (TNK-tPA) is equivalent to t-PA in 30 days mortality but associated with significantly lower rate of non-cerebral bleeding and need for blood transfusion.

Give fibrinolytic therapy to elderly if → Mechanical reperfusion can not be performed.

Re-administer fibrinolytic therapy except for streptokinase and Anistreplase if → Re-occlusion or reinfarction with recurrence of ST-segment elevation or BBB and mechanical reperfusion is not available.

Give weight-adjusted iv Heparin with fibrinolytics especially Alteplase. Continue Heparin for 24-48 hours after fibrinolysis.

Heparin is optional with Streptokinase (subcutaneous or iv). (ESC, 2003)

Give Heparin with streptokinase in patients at high risk for systemic emboli (large or anterior MI, AF previous emboli). (ACC/AHA, 1999)
Routine use of reduced dose of fibrinolytic therapy with GP IIb/IIIa inhibitors is still not recommended. (ESC, 2003)

Fibrinolytic Regimens in AMI:

Streptokinase: 1.5 million units in 100 ml of 5% dextrose or 0.9% saline over 30-60 minutes.

Alteplase: 15 mg iv bolus, then 0.75 mg/kg over 30 minutes, then 0.5 mg/kg over 60 min iv. Total dosage should not exceed 100 mg.

Reteplase (rPA) 10 U and 10 U iv bolus given 30 min apart.

Tenecteplase (TNK-tPA) single iv bolus of:
- 30 mg if < 60 kg.
- 35 mg if 60 to < 70 kg.
- 40 mg if 70 to < 80 kg.
- 45 mg if 80 to < 90 kg.
- 50 mg if > 90 kg.

Heparin Regimen:

Intravenous bolus 60 U/kg with max 4000 unit.
Intravenous infusion: 12 U/kg with a max of 1000 U/hr for 24-48 hours. (ESC, 2003)
Heparin is administered as continuous infusion. (Consensus Panel, Micromedix, 2003)

Monitor Heparin closely → aPTT at 3, 6, 12, 24 hrs after starting weight-adjusted Heparin
Target aPTT = 70 s.
/aPTT > 70 s is associated with higher mortality, bleeding or reinfarction. (ESC, 2003)

Low-Molecular Weight Heparin:

ASSENT-3 trial → Enoxaparin with Tenecteplase → 30 mg iv bolus, followed by SC injection 1 mg/kg every 12 hours, for a maximum of 7 days. (ESC, 2003; ASSENT-3, 2001)
**Side Effects of Fibrinolytics:**

1- Intra-cranial haemorrhage.

2- Stroke.

3- Non-cerebral bleeding: mainly procedure-related. May require blood transfusion or can be life threatening.

4- Hypotension: stop the infusion temporarily, lay the patient flat or elevate the feet. Atropine or iv volume expansion may be required.

5- Allergic reactions: rare. Routine use of hydrocortisone is not indicated.

**Contraindications:**

*Absolute:*

1- Haemorrhagic stroke or stroke of unknown origin at any time.

2- Ischemic stroke in the preceding 6 months.

3- Central nervous system damage or neoplasm.

4- Recent major trauma/surgery/head injury (within preceding 3 weeks).

5- Gastro-intestinal bleeding within the last month.

6- Known bleeding disorder.

7- Aortic dissection.  

*(ESC, 2003)*

*Relative:*

1- Transient ischemic attack in preceding 6 months.

2- Oral anticoagulant therapy.

3- Pregnancy or within 1 week postpartum.

4- Traumatic resuscitation.

5- Refractory hypertension (systolic blood pressure > 180 mmHg).

6- Advanced liver disease.

7- Infective endocarditis.

8- Active peptic ulcer.  

*(ESC, 2003)*

**2.3- Rescue PCI:**

If thrombolysis fails with fibrinolytics → PCI.
3- Management of Immediate Complications during Acute Phase:

If patient develops:

1- **Hyperdynamic state:** (tachycardia, loud heart sounds and good peripheral circulation):
   Give Beta-blockers.

2- **Bradycardia-hypotension:** (bradycardia, venodilatation, decreased tissue perfusion).
   Give Atropine or pacing.

3- **Hypovolemia:** (veno-constriction, poor tissue perfusion):
   Give fluid infusion.

4- **Right ventricular infarction:** (bradycardia, hypotension, poor tissue perfusion)
   Avoid (if possible) vasodilator drugs e.g Opioids, Nitrates, Diuretics and ACE-Inhibitors.

   Administer fluid loading ➔ Initially rapid administration of 200 ml in 10 min.
   To maintain ventricular preload ➔ Give infusion of 1-2 L normal saline in first few hours then 200 ml/hr thereafter.
   (ESC, 2003)

   If iv fluids fail give Dobutamine infusion (2-15 mcg/kg/min). (Consensus Panel)

   Monitor hemodynamic status carefully during iv fluid loading.
   If atrial fibrillation occurs ➔ correct promptly.
   If hypotensive patient ➔ fibrinolytic therapy. Alternatively direct PCI rapidly corrects hemodynamic status.
   (ESC, 2003)

5- **Heart failure:**

   **Mild and moderately severe heart failure:**
   Oxygen therapy, use with caution in obstructive pulmonary disease.
Furosemide: 20-40 mg iv repeated at 1-4 hours interval if necessary if no response give iv or oral Nitrates if no hypotension (monitor blood pressure during dose titration to avoid hypotension).

Initiate ACE-Inhibitors within 48 hours of MI in the absence of hypotension, hypovolemia, or renal failure.

**Severe heart failure:**

Oxygen therapy.

Furosemide: 20-40 mg iv repeated at 1-4 hours interval if necessary.

Give iv GTN if no hypotension starting at 0.25 mcg/kg/min, increase every 5 minutes until fall in blood pressure by 15 mmHg or SBP < 90 mmHg.

If hypotension or signs of renal hypoperfusion give dopamine iv 2.5 – 5 mcg/kg/min.

If pulmonary congestion is dominant give Dobutamine iv initially at 2.5 mcg/kg/min, can be increased at 5-10 min interval up to 10 mcg/kg/min or until hemodynamic improvement.

Ventilatory support if inadequate oxygen tension.

Consider early revascularization if not available give fibrinolytic therapy.

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**6- Cardiogenic shock** (Hypoperfusion, SBP < 90 mm Hg)

Oxygen therapy.

Inotropic agents: Dopamine initially 2.5-5 mcg/kg/min, gradual up-titration of doses to 15-20 mcg/kg/min (until systemic BP > 90-100 mmHg).

If higher dopamine doses are required give norepinephrine infusion 0.02-0.04 mcg/kg/min.

Dobutamine (5-10 mcg/kg/min) is the preferred agent if systemic BP > 90 mmHg.

Maintain systemic BP > 90 mmHg. (Consensus panel)

Ventilatory support if inadequate oxygen tension.

Consider emergency PCI, if not available give fibrinolytic therapy. (ESC, 2003)
Other Complications during Acute-Phase after MI are:

A- Arrhythmias and Conduction Disorders:

I. Ventricular Arrhythmias:

1- Ventricular Ectopic Rhythms: no specific therapy is required.

2- Ventricular Tachycardia:
   If prolonged leading to hypotension, heart failure or ventricular fibrillation ➔
   Give Beta-blockers unless contraindicated.
   If high risk for recurrent ventricular fibrillation ➔ iv Lidocaine: initial loading
dose: 1 mg/kg. Followed by 0.5 mg/kg iv every 8-10 minutes to a maximum of
   4 mg/kg or continuous infusion (1-3 mg/min). (ESC, 2003)

   If recurrent sustained ventricular tachycardia requiring cardioversion or
   ventricular fibrillation ➔ iv Amiodarone 5 mg/kg in first hour, followed by 900-
   1200 mg/24 hr.

3- Ventricular Fibrillation. Immediate defibrillation.

II. Supraventricular Tachycardia:
Atrial fibrillation: usually no treatment required.

If contributes to heart failure ➔ Amiodarone (more effective in terminating arrhythmia).
   Beta-blockers and Digoxin (slowing rate).
Verapamil is not recommended. (ESC, 2003)

Heparin should be given. (ACC/AHA, 1999)

III. Sinus Bradycardia and Heart Block:
If sinus bradycardia accompanied by severe hypotension ➔ iv Atropine initially (0.6-1
mg, repeated up to total of 2 mg (or 0.04 mg/kg). (Consensus panel)
If Atropine fails ➔ Pacing.
First degree block → no treatment required.
Second degree AV block: (type I) if associated with hemodynamic effects → Atropine if fails → pacing. (ESC, 2003)

4- Routine Prophylactic Therapies in the Acute Phase:

4.1- Aspirin:
Give Aspirin to all patients with AMI as soon as possible after diagnosis unless contraindicated. (Mentioned above)

Contraindications:
Hypersensitivity- bleeding peptic ulcer – blood dyscrasia – severe hepatic disease – bronchospasm in asthma (occasional).

4.2- Antiarrhythmic drugs:
Routine use of Lidocaine to control ventricular fibrillation is not recommended. (ESC, 2003)

4.3- Beta-blockers:
Give Beta-blockers within 12 hours of onset of MI, in the absence of contraindications and severe LVSD. (ACC/AHA, 1999)

Routine early use of iv Beta-blockers is not recommended. Usually oral Beta-blockers will suffice in most patients.

Give iv Beta-blockers if → 1- Pain unresponsive to opioids. 2- HTN. 3- Tachycardia in absence of HF. (ESC, 2003)

Dosing of iv Beta-blockers in the Acute Phase:
Atenolol: 5 mg iv injection over 5 minutes, then 50 mg orally after 10-15 minutes, then 50 mg after 12 hours, then start maintenance dose of 100 mg daily.
Metoprolol: 5 mg by iv injection every 2 minutes to a maximum of 15 mg, followed after 15 minutes by 50 mg orally every 6 hours for 2 days, then start maintenance dose of 200 mg daily in divided doses. (BNF, 2002)
4.4- Nitrates:
Routine use of Nitrates in the early phase of MI is not recommended.

Give Nitrates if Pain unresponsive to Opioids. (ESC, 2003)

**Dosing of iv Nitrates in the acute phase:**
GTN: iv infusion of 10-200 mcg/min.
Isosorbide dinitrate: iv infusion 2-10 mg/hr, can be given up to 20 mg/hr. (BNF, 2002)

4.5- Calcium Channel Blockers:
Not recommended in the acute phase of MI.

4.6- ACE-Inhibitors:
Give ACE-Inhibitors to all MI patients, particularly those with high risk (impaired EF, HF in the early phase, anterior MI, high heart rate, previous MI, DM, HTN).

(Franzosi et al, 1998; ESC, 2003; Consensus panel)

ACE-Inhibitors should be started within the first 24 hours in the absence of contraindications (hypotension SBP< 100 mmHg, cardiogenic shock). (ESC, 2003)

**Dosing:**

**Captopril**
Initially 6.25 mg, increase over several weeks up to 150 mg/day (if tolerated in divided doses).

**Lisinopril**
Initially 5 mg within first 24 hrs, followed by 5 mg in second day, then 10 mg in third day, maintain on 10 mg once daily.
If SBP < 100 mmHg do not start medication.
If SBP = 100-120 mmHg ➔ initiate on 2.5 mg increasing to Maintenance dose of 5 mg once daily.
If SBP drops to < 100 mmHg during therapy ➔ reduce to 5 or 2.5 mg.
If prolonged hypotension SBP <90 mmHg for > 1 hr ➔ stop drug.
Ramipril Initially 2.5 mg twice daily → increase after 2 days to 5 mg twice daily. Maintenance dose 2.5-5 mg twice daily.

Trandolapril Initially 500 mcg daily → increase gradually to a max 4 mg/day. If symptomatic hypotension develops → stop dose up-titration. Reduce dose of adjunctive therapy → If ineffective reduce dose of Trandolapril.

Enalapril Initially 2.5 mg. Maintenance dose 5-20 mg PO daily. (BNF, 2002; ESC, 2003)

Check renal function prior to initiation of drug and after each significant dose increase. (NICE, 2003)

4.7- Magnesium:
Magnesium therapy has no benefit in MI.

4.8- Glucose- Insulin-Potassium:
Limited evidence that routine administration of Glucose-Insulin-Potassium decreases mortality. However, use of this treatment still awaits results of a large ongoing mortality trial. (ESC, 2003)

5- Later In-Hospital Care:
Goals: Management of ensuing in-hospital complications.

*Deep Vein Thrombosis and Pulmonary Embolism:*
Uncommon except in patients kept in bed for long time because of HF. For prevention → Give prophylactic doses of LMWH. If DVT occurs → Give therapeutic doses of LMWH followed by oral anticoagulation for 3-6 months.
**Intra-ventricular Thrombus and Systemic Emboli:**
Give iv Heparin or LMWH initially, then oral anticoagulation for 3-6 months.

**Pericarditis:**
If pain is troublesome ➔ Give high dose oral or iv Aspirin, NSAIDs or steroids.

**Late Ventricular Arrhythmias:**
If ischemia-induced ➔ Consider revascularization by PCI or surgery.

If not ischemia-induced ➔ Use of Beta-blockers, Amiodarone, electro-physiologically guided antiarrhythmic therapy and/or insertion of an implantable converter defibrillator.

**Post-Infarction Angina and Ischemia:**
If recurrent or inducible angina (due to re-occlusion or re-stenosis) ➔ PCI or CABG.
ESC, 2003

6- Secondary Prevention and Prophylaxis Post Infarction:
**Goals:** Prevent progression of coronary artery disease, new infarction, heart failure and death.

6.1- Smoking Cessation.

6.2- Diet and Dietary Supplements.
- Mediterranean-type diet: low in saturated fat, high in poly-unsaturated fat, fruit and vegetables.
- Give Supplements of fish oil n-3 polyunsaturated fatty acids 1 gm daily.

6.3- Optimal Glycaemic Control in Diabetic Patients.

6.4- Blood Pressure Control in Hypertensive Patients.
6.5- Antiplatelet and Anticoagulant Treatment:

- Aspirin: 75 – 325 mg daily.
- Lower doses 75-160 mg are effective with fewer side effects.
- Oral anticoagulants have no benefit over Aspirin even when combined → Routine use of anticoagulants after AMI is not recommended at present.
- Consider oral anticoagulants if Aspirin is not tolerated.
- Routine use of Clopidogrel along with Aspirin following reperfusion therapy is not recommended at present.*
- Use Clopidogrel (75 mg) if Aspirin is not tolerated.

6.6- Beta-blockers:

- Give oral Beta-blockers indefinitely after AMI to all patients if no contraindications.
- Agents of choice: Propranolol, Atenolol, Metoprolol, Timolol and Carvedilol. Evidence for other Beta-blockers is less convincing. (ESC, 2003)
- Avoid Beta-blockers with intrinsic sympathomimetic activity. (Freemantle et al, 1999)

**Dosing:**

Propranolol 40 mg 4 times daily for 2-3 days, then 80 mg twice daily

Metoprolol 200 mg daily in doses.

Timolol Initially 5 mg twice daily for 2 days, increase to 10 mg twice daily

Atenolol 100 mg daily in 1 or 2 doses. (BNF, 2002)

Carvedilol Initially 6.25 mg twice daily → If no adverse effects, HR > 50 bpm and SBP > 80 mmHg → increase dose to a maximum of 25 mg twice daily over 4-6 weeks. (CAPRICORN trial, 2001)

* “Current evidence supports dual anti-platelet therapy for long-term treatment (at least 12 months) in patients with ACS after PCI, after which Aspirin is continued indefinitely. Longer-term Clopidogrel should be considered based on patient risk”*. Source: Jneid at al, 2003. The present literature does not highlight dual antiplatelet therapy in ST-segment Elevation MI (including those undergoing PCI).
6.7- Calcium Channel Blockers:
Give CCB (Verapamil or Diltiazem) if Beta-blockers are contraindicated (especially in obstructive airway disease) and no HF.

Diltiazem: 300 mg daily.  
Verapamil: 120 mg 2-3 times daily.  

(DAVIT trial, 1984; DAVIT II, 1990; Jespersen, 1993; Hansen et al, 1997)

Do not give dihydropyridines unless there is clear indication (no evidence they improve prognosis after MI).

6.8- Nitrates:
Do not give Nitrates in the absence of angina (no evidence they improve prognosis post MI).

ISDN orally 5-80 mg 2-3 times daily.
SL 5-10 mg PRN
GTN SL 0.3-1 mg PRN

6.9- ACE-Inhibitors:
• Continue ACE-Inhibitors started on first day in all patients in absence of contraindications.
• Continue administration of ACE-Inhibitors for at least 4-5 years even in absence of ventricular dysfunction (maybe indefinitely).

6.10- Lipid-lowering Drugs:
Goal LDL level is < 100 mg/dl.  

(NCEP/ ATP III, 2002)

For all patients obtain fasting lipoprotein profile (LDL, HDL, TG, total Cholesterol) upon admission or within 24 hours, before administration of lipid-lowering medication.
If LDL \( \geq 130 \text{ mg/dl} \) \( \Rightarrow \) Give LDL-lowering drugs.

If LDL = 100-129 mg/dl \( \Rightarrow \) Several therapeutic options are available:

1- Start LDL-lowering therapy (advisable).

2- Postpone therapy until therapeutic life changes measures are taken (weight reduction, smoking cessation, increase physical activity, dietary changes) \( \Rightarrow \) if <100 mg/dl could not be achieved then use drug therapy.

3- Treatment of other lipid or non-lipid risk factors: consider use of Nicotinic acid or Fibrates for elevated triglycerides or low HDL cholesterol. In addition to control of HTN and hyperglycaemia. (NCEP/ATP III, 2002; ACC/AHA, 2002)

If LDL < 100 mg/dl \( \Rightarrow \) LDL-lowering therapy is not required, and attention shifts to other lipids if TG > 200 mg/dl or HDL < 40 mg/dl.

Statins are the first line drugs to lower LDL (Administered with evening meal or at bedtime).

If transaminases increase more than 3 times the upper limit of their normal range \( \Rightarrow \) Discontinue therapy. Monitor liver transaminases (ALT and AST) before and within 1-3 months of starting therapy, BNF 2002).

If Myopathy \( \Rightarrow \) Discontinue therapy.

Bile acid sequestrants are the second line drugs to lower LDL. Consider them if:

1- Moderate elevation in LDL.
2- Younger persons with elevated LDL
3- Women with elevated LDL considering pregnancy.

If TG level > 400 mg/dl \( \Rightarrow \) Do not give Bile acid sequestrants as monotherapy (only when TG < 200 mg/dl).

If Bile acid sequestrants are administered \( \Rightarrow \) Give other drugs one hour before or 4 hours after their administration.
Consider Bile acid sequestrants in combination with Statins \( \Rightarrow \) in very high LDL-cholesterol level.

Consider Fibrates primarily in patients with high TG, high B-VLDL, low HDL and LDL near optimal.

Nicotinic acid is the most effective lipid-lowering drug for raising HDL cholesterol. Consider Nicotinic acids in patients with low HDL, high TG, and moderately high LDL.

It is not recommended to switch from one preparation to another, because of considerable variations between different sustained-release preparations in terms of pharmacokinetics, efficacy, safety profile and adverse drug reactions.

\( \text{(NCEP/ATP III, 2002; Pieper, 2003; Pieper, 2002)} \)

Nicotinic acids can be combined with Statins \( \Rightarrow \) further decrease in LDL.

**Table: Lipid/lipoprotein effect of the different lipid-lowering drugs:**

\( \text{(NCEP/ATP III, 2002)} \)

<table>
<thead>
<tr>
<th></th>
<th>Statins</th>
<th>Bile Acids</th>
<th>Nicotinic Acid</th>
<th>Fibrates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LDL</strong></td>
<td>118-55%</td>
<td>115-30%</td>
<td>15-25%</td>
<td>15-20%</td>
</tr>
<tr>
<td><strong>HDL</strong></td>
<td>15-15%</td>
<td>13-5%</td>
<td>15-35%</td>
<td>10-35%</td>
</tr>
<tr>
<td><strong>TG</strong></td>
<td>17-30%</td>
<td>No effect or ↓</td>
<td>120-50%</td>
<td>120-50%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Doses:</strong></th>
<th><strong>Initial dose</strong></th>
<th><strong>Maximum FDA-approved dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20 mg</td>
<td>80 mg (Max 10 mg daily with concomitant Ciclosporin, Fibrates, or lipid-lowering dose of Nicotinic acid; BNF, 2002)</td>
</tr>
</tbody>
</table>
Fluvastatin 20 mg (40mg) 80 mg

Atrovastatin 10 mg 80 mg (NCEP/ATP III, 2002)

Fibrates:  
Usual daily dose  Maximum dose

Gemfibrozil  600 mg twice/day  1200 mg

Fenofibrate  200 mg once daily  200 mg

Clofibrate  1000 mg twice/day  2000 mg (NCEP/ATP III, 2002)

Bile acid sequestrants:  
Usual daily dose  Maximum dose

Cholestyramine  4-16 g  24 g

Colestipol  5-20 g  30 g

Colesevelam  2.6-3.8 g  4.4 g (NCEP/ATP III, 2002)

Nicotinic Acid:  
Usual daily dose  Maximum dose

Crystalline  1.5-3 g  4.5 g

Sustained-release  1-2 g  2 g

Extended release  2 g  2 g (NCEP/ATP III, 2002)

Contraindications

Statins:
Absolute: Active or chronic liver disease.
Relative: concomitant use of Ciclosporin, macrolide antibiotics, antifungal agents and cytochrome P-450 inhibitors (Fibrates and Nicotinic acid should be used with caution).
**Fibrates:** Severe hepatic or renal insufficiency.

**Bile acid sequestrants:**
Absolute: Familial dysbeta-lipoproteinemia, TG > 400 mg/dl.
Relative: TG >200 mg/dl.

**Nicotinic acid:**
Absolute: Chronic liver disease, severe gout.
Relative: hyperuricemia, high doses in DM type II. (NCEP/ATP III, 2002)

**Major Side Effects:**
**Statins:** Myopathy and increased liver transaminases.
**Fibrates:** Dyspepsia, various upper GI complaints, cholesterol gallstones, and myopathy.
**Bile acid sequestrants:** Upper and lower gastrointestinal complaints, decreased absorption of other drugs.
**Nicotinic acid:** Flushing, hyperglycemia, hyperuricemia or gout, upper GI distress, hepato-toxicity, especially with sustained-release form. (NCEP/ATP III, 2002)
References:


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The School of Pharmacy  
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Template on the Management of Heart Failure  
Locally Adopted to the Jordanian Settings

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This template presents recommendations by ACC/AHA on drug-use and therapy monitoring in heart failure (HF). The New Zealand guidelines for management of heart failure are used to complement template. Drug doses and contraindications are abstracted from the BNF, September 2002.

Recommendations presented herein do not override or replace clinical judgement of health care professionals in light of patient circumstances.

**Management of Heart Failure (HF):**

1. **General Measures:**
   1.1 **Control systolic and diastolic hypertension (HTN).**
   a- Give preference to drugs that can control both HTN and HF, such as Diuretics, ACE-inhibitors and Beta-blockers.
   b- Avoid Calcium channel blockers (CCB) because of their cardiodepressant effect, except Amlodipine.
   c- Avoid potent direct-acting vasodilators, such as Minoxidil because of Sodium retention.

   1.2- **Control hyperglycaemia.**
   a- It is not recommended to avoid Beta-blockers in DM. Cardio-selective agents are preferred.
   b- Use Thiazolidinedione (oral hypoglycaemic agent) with caution because it leads to fluid retention and weight increase.

   1.3- **Control hyperlipidemia.**

   1.4- **Treat thyroid disorders, hypo- or hyperthyroidism, anaemia, infections.**

   1.5- **Encourage physical activity** in all stable patients with chronic heart failure in conjunction to therapy. Avoid in periods of decompensation or in patients with suspected myocarditis. (ACC/AHA, 2001)
2. Drug Therapy of HF:

**Recommended Drug-use Practice:** (This encompasses practice for which: 1- Evidence and/or general agreement that therapy is effective and useful exists. 2- Conflicting evidence and/or divergence in opinion about efficacy and usefulness of therapy exists, but more in favour of usefulness and efficacy).

2.1 Diuretics:

Give Loop Diuretics to all HF patients with history or current evidence of fluid retention.

Loop Diuretics are preferred in most HF patients over Thiazide, Metolazone and Potassium sparing diuretics (Spironolactone). Most common is Furosemide, some patients respond better to Torasemide. (ACC/AHA, 2001)

Do not give Thiazide Diuretics in poor renal function (creatinine clearance < 30 ml/min). (ineffective). (BNF, 2002)

**Initiation and Maintenance:**

1- Start at low doses, then up-titratre dose until urine output increases and weight decreases by 0.5- 1 kg/day. Increase dose or frequency to maintain weight loss and active diuresis. Adjust dose to reach target euvolemia. Avoid volume depletion (with high doses) or retention (with inappropriately low doses).

2- Maintain Diuretic therapy even after resolution of fluid retention.

**Dosing:**

Furosemide: edema: Orally: Initial dose: 40 mg in the morning. (In ACC/AHA 20-40 mg once or twice daily).

Maintenance dose: 20 mg daily or 40 mg on alternate days 80 mg or more in resistant edema.

Maximum dose: not stated in BNF. But in ACC/AHA it is up to 400 mg daily.

iv injection 20-50 mg (slowly).
iv infusion  rate not exceeding 4 mg/min.

Bumetanide: edema  Orally: Initial dose: 1 mg in the morning, repeated after 6-8 hours if needed.
In severe cases: increase to 5 mg or more daily.
In elderly: 0.5 mg daily.
Maximum dose not stated in BNF, but in ACC/AHA it is 10 mg daily.
iv injection  1-2 mg repeated after 20 minutes.
iv infusion  2-5 mg over 30-60 minutes.

Metolazone: edema  Orally:  5-10 mg (in the morning).
In resistant edema: increase to 20 mg daily.
Maximum dose: 80 mg daily.

Hydrochlorothiazide: dose is not stated in the BNF nor ACC/AHA.  (BNF, 2002)

Management of Diuretic-induced adverse effects:
If hypotension or azotemia: (particularly in patients on high dose Diuretic ≥ 80 mg daily).
If no signs of fluid retention → Decrease Diuretic dose. Do not stop drug.

If signs of fluid retention exist → Maintain Diuretic dose and improve end-organ perfusion (Use ACE-Inhibitors, Digoxin, Beta-blockers)

If resistant edema → Administer Diuretics intravenously,
   OR  Combine 2 or more Diuretics example: Furosemide and Metolazone.
   OR  Use Diuretics with a positive inotropic agent (preferably Milrinone).

If Potassium depletion occurs → Give short-term Potassium supplements.
If severe Potassium depletion → Give Magnesium and Potassium supplements.
If Potassium supplements are given with ACE-Inhibitors and/or Spironolactone → Use cautiously.  (ACC/AHA, 2001)
**Contraindications:**

1- **Loop Diuretics:** Renal failure with anuria (Furosemide and Torasemide), pregnancy and breast-feeding (Torasemide).

2- **Thiazides:** Refractory hypokalemia, hyponatremia, hypercalcemia, severe renal and hepatic impairment, symptomatic hyperuricemia, Addison’s disease. (BNF, 2002)

Do not use Diuretics alone ➔ Combine with ACE-Inhibitor, Beta-blockers (and Digoxin) (Even if patient responded favourably to therapy)

- Ensure appropriate Diuretic dose (no or minimal fluid retention) before and during ACE-Inhibitor and Beta-blocker therapy. (ACC/AHA, 2001)

2.2 **ACE-Inhibitors and Beta-blockers:**

Give ACE-Inhibitors and Beta-blockers routinely to all HF patients due to LVSD unless contraindicated or intolerated. Do not delay treatment even if mild symptoms exist.

ACE-Inhibitors and Beta-blockers combined give an additive effect. Addition of Beta-blocker to a low dose of ACE-Inhibitor produces greater improvement of symptoms and decreases risk of death over increasing the dose of ACE-Inhibitor even to target doses.

Give preference to Captopril, Enalapril, Lisinopril and Ramipril.

Both Beta1-selective (Metoprolol, Bisoprolol) and non-selective (Propranolol, Carvedilol) Beta-blockers are effective in treatment of HF. Esmolol and Sotalol are used for the management of arrhythmias only.

ACE-Inhibitors are preferred over ARBs or vasodilators such as Isosorbide dinitrate and Hydralazine (because of better survival rates).

**Give ACE-Inhibitors and Beta-blockers:**

1- With or without Cardiovascular risk factors, DM, CAD, HTN.

2- Recent or remote history of MI regardless ejection fraction.

3- Reduced ejection fraction regardless MI presence.
Delay initiation of Beta-blockers if:

1. Evidence of fluid retention or depletion (as it may induce severe hypotension).
2. Unstable HF.
3. Recent treatment with intravenous positive inotropic agent.

Stabilize patient using other therapy such as Diuretics, then re-consider Beta-blocker therapy. (ACC/AHA, 2001)

Give ACE-Inhibitors with caution in:

1. Hypotension (SBP < 80 mmHg).
2. Renal impairment, (serum creatinine > 3 mg/dl).
3. Hyperkalaemia (Serum K > 5.5 mmol/L), Hyponatraemia (Na < 130 mmol/L).
4. High dose vasodilator therapy.
5. Multiple or high dose Diuretic therapy especially with low-Sodium diet, dialysis, or dehydration.
6. Age 70 years or more.
8. Unstable HF (Low BP, Systemic hypoperfusion).
9. Severe generalized atherosclerosis or peripheral vascular diseases (owing to risk of clinically silent renovascular diseases). (BNF, 2002)

Stop ACE-Inhibitor therapy temporarily if: Hemodynamically or clinically unstable (Decrease or skip dose) patients, (especially those poorly responding to Diuretics), until patient is stabilized.

Discontinue ACE-Inhibitors if:

1. Angioedema
2. Anuric renal failure.

Discontinue Beta-blockers temporarily if: Hypoperfusion or need for positive inotropic agent occurs (Dobutamine, Dopamine, Milrinone).
Once stabilized re-consider Beta-blockers.

Avoid abrupt cessation of ACE-Inhibitors or Beta-blockers, unless there is life-threatening condition such as angioedema in case of ACE-Inhibitors. (ACC/AHA, 2001)
**Initiation and Maintenance of ACE-Inhibitors and Beta-blockers:**

Initiate ACE-Inhibitors and Beta-blockers therapy with low doses, if well-tolerated. Increase gradually to achieve doses used in clinical trials, unless intolerated.

If fluid retention occurs on initiation of Beta-blockers, increase dose of Diuretic and continue giving Beta-blockers.

Maintain ACE-Inhibitors and Beta-blocker therapy even if mild symptoms sustain or patient does not benefit symptomatically. (ACC/AHA, 2001)

**Dosing:**

1. **ACE-Inhibitors:** Dose is titrated to a target dose (or the maximum tolerated dose if lower).
   - **Captopril:** Initial dose: 6.25 x 3 once daily. Maintenance dose: 25 mg 2-3 times daily. Target dose: 50 mg three times daily. Maximum dose: 150 mg daily.
   - **Cilazapril:** Initial dose: 500 microgram once daily. Maintenance dose: 1-2.5 mg daily. Maximum dose: 5 mg daily. Target dose: Not stated.
   - **Enalapril:** Initial dose: 2.5 x 2 mg daily. Maintenance dose: 10-20 mg daily in 1-2 divided doses. Target dose: 20 mg twice daily. Maximum dose: 20 mg twice daily. (ACC/AHA, 2001)
   - **Fosinopril:** Initial dose: 10 mg daily. If well tolerated increase dose. Maximum dose: 40 mg once daily. Target dose: 40 mg.
Lisinopril  Initial dose: 2.5 mg daily.
Maintenance dose: 5-20 mg daily.
Target dose: 40 mg daily.
Maximum dose: 40 mg once daily.  (ACC/AHA, 2001)

Perindopril  Initial dose: 2 mg in the morning.
Maintenance dose: 4 mg once daily (before food).

Ramipril  Initial dose: 1.25-2.5 mg once daily.
Maximum dose: 10 mg once daily.  (BNF, 2002)

2- Beta-blockers:

Carvedilol:  Initial dose: 3.125 mg twice daily (with food).
Dose increased at intervals of at least 2 weeks to 6.25 mg twice daily,
then 12.5 mg twice daily, then to 25 mg twice daily.
Maximum dose: 25 mg x 2 daily in severe heart failure and body weight <
85 kg, or 50 mg x 2 daily in severe heart failure and Body weight > 85 kg.

Bisoprolol:  Initial dose: 1.25 mg once daily (in the morning) for one week.
Up-titration: 2.5 mg once daily for one week, then 3.75 mg once daily
For one week, then 5 mg once daily for 4 weeks, then 7.5 mg once daily
for 4 weeks, then 10 mg once daily.
Maximum dose: 10 mg once daily.  (BNF, 2002)

Metoprolol tartrate:  Initial dose: 6.25 mg twice daily.
Maximum dose: 75 mg twice daily.

Metoprolol Succinate:  Initial dose: 12.5 to 25 mg daily.
(Extended release) Maximum dose: 200 mg once daily.  (ACC/AHA, 2001)
**Jordanian Practice:** Start with a short acting Beta-blocker (e.g. Metoprolol), if well-tolerated switch to long-acting Beta-blocker (e.g. long-acting Metoprolol, Carvedilol or Bisoprolol). (Consensus panel)

Dose reduction may be necessary in renal impairment for water-soluble Beta-blockers.

**Management of ACE-Inhibitors or Beta-blockers Induced Adverse Effects:**

If hypotension occurs with ACE-Inhibitors, Reduce dose of Diuretic, or especially first dose or when increasing doses Liberalize Sodium intake, or provided that there is no significant fluid retention Both.

If hypotension occurs with concomitant Administer at different timing, If ineffective Beta-blocker and ACE-Inhibitors Reduce temporarily dose of ACE-Inhibitors, or Diuretics dose (if no fluid retention).

(ACC/AHA, 2001)

If azotemia or serum creatinine levels increase with ACE-Inhibitors:

- If no fluid retention Decrease the concomitantly administered Diuretic dose.
- If fluid retention exists and dose of Diuretics cannot be reduced The physician and patient may need to tolerate mild to moderate degrees of azotemia to maintain ACE-Inhibitor therapy.

If persistent, non-productive cough with ACE-Inhibitors:

Rule out other causes before withdrawal of ACE-Inhibitors (respiratory diseases).

If tolerable encourage patients to continue ACE-Inhibitors.

If severe use alternatives as ARBs.

If bradycardia or heart block occur with Beta-blockers:

- Rule out drug interactions, and consider discontinuing causative drugs.
- If they are Beta-blocker induced Reduce Beta-blocker dose if:
  1- Bradycardia is associated with dizziness or lightheadedness.
  2- Second or third degree heart block occurs.
Beta-blockers with intrinsic sympathomimetic activity cause less bradycardia and coldness of extremities than other Beta-blockers. (BNF, 2002)

If fatigue occurs with Beta-blockers ➔ No intervention (resolves spontaneously after several weeks)
If severe ➔ Reduce Beta-blocker dose (or Diuretic dose)
If accompanied with peripheral hypoperfusion ➔ Discontinue Beta-blockers.

(ACC/AHA, 2001)

Fatigue and coldness of extremities maybe less common with Beta-blockers of ISA
Sleep disturbances and nightmares are less with water soluble Beta-blockers.

(BNF, 2002)

DM is not a contraindication to Beta-blockers, but use with caution in IDDM.

Carvedilol is preferred in DM, because it increases insulin sensitivity and improves lipid profile. (Consensus panel; Jacob et al, 1996; Jacob et al, 1998)

**Contraindications:**

1- **ACE-Inhibitors:**
1- Severe hypotension and immediate risk of cardiogenic shock, until patient is stabilized, then re-evaluate for ACE-Inhibitors (ACC/AHA).
2- Severe bilateral renal stenosis (or severe stenosis of artery supplying single kidney).
3- Angioedema. 4- Pregnancy. 5- Aortic stenosis. 6- Porphyria

To prevent anaphylactoid reactions avoid ACE-Inhibitors:
1- During dialysis with high-flux polyacrylonitrile membranes, and low density lipoprotein apheresis with dextran sulphate.
2- Before desensitization with wasp or bee venom. (BNF, 2002)

2- **Beta-blockers:**
1- Asthma and COPD. (Differs from ACC/AHA where COPD is not a contraindication).
If no alternative use a cardio-selective agent (Bisoprolol, Metoprolol, and to a lesser extent Acebutolol) with caution.
2- Hypotension.  
4- Sick sinus syndrome.  
6- Marked symptomatic bradycardia.  
8- Cardiogenic shock.  
10- Severe peripheral vascular diseases.  
11- Pheochromocytoma (not a contraindication to alpha and Beta blockers).

(BNF, 2002)

2.3 Digitalis:
Consider Digitalis for treatment of symptoms in conjunction with ACE-Inhibitors, Beta-blockers and Diuretics unless contraindicated.

*Initiation and Maintenance:*

Digoxin may be used either:

1- Early to reduce symptoms in patients who have been receiving but have not yet responded symptomatically to, ACE-Inhibitors or Beta-blockers.

Or 2- Delayed until response to ACE-Inhibitors and Beta-blockers has been defined and used only in patients who remained symptomatic despite therapy.

*Dosing:*

Digoxin usually initiated and maintained at: 0.125 - 0.25 mg daily. No need for loading dose in HF patients to initiate therapy.

Use low doses of 0.125 mg daily or (every other day) in:

1- Elderly patients over 70 years old.  
2- Low lean body mass.  
3- Impaired renal function.  
4- Hypokalemia or hypothyroidism.  
5- Hypomagnesaemia.

Higher doses: 0.375-0.5 mg daily are rarely used.

If patient is on Digoxin and no ACE-Inhibitors or Beta-blocker ➔ Add these drugs, without stopping Digoxin.

Use Digoxin cautiously if ➔ Given with concomitant therapy that can induce SA or AV function depression, such as Amiodarone and Beta-blockers.
Decrease Digoxin dose if Quinidine, Amiodarone, Propafenone, Verapamil, Flecanide, or Spironolactone are initiated.

In acutely decompensated HF Do not use Digoxin as a primary therapy. First stabilize with appropriate treatment, usually iv medication. Then consider Digoxin in long term therapy. (ACC/AHA, 2001)

**Signs of Digoxin Toxicity:**
Nausea, vomiting, diarrhoea, abdominal pain, visual disturbances, headache, fatigue, drowsiness, confusion, hallucination, insomnia, restlessness, arrhythmias, and heart block. (BNF, 2002)

**Contraindications:**
1. Intermittent complete heart block.
2. Second degree AV block (unless treated with pace-maker).
4. Hypertrophic obstructive cardiomyopathy (unless accompanied by AF and HF) but with caution.

**2.4 Milrinone:**
A phosphodiesterase (positive inotropic drug). It is indicated as a short-term treatment in severe congestive HF unresponsive to maintenance therapy and in acute HF.

Dose: iv injection (dilute before use) 50 microgram/kg over 10 minutes. Followed by:
- iv infusion 375-750 ng/kg/min, for 48 -72 hours in CHF.
- Maximum daily dose: 1.13 mg/kg. (BNF, 2002)

**2.5 Potassium-Sparing Diuretics:**
Use Spironolactone in patients with symptoms at rest (severe HF) despite use of ACE-inhibitors, Beta-blockers, Digoxin and Diuretics, with preserved renal function and normal Potassium level.

Spironolactone can not yet be recommended in mild to moderate HF.
Stop Potassium supplements when starting therapy with Spironolactone.

Reduce Spironolactone dose → If Potassium level > 5.4 mmol/L.

Stop Spironolactone if → Serious hyperkalaemia or painful gynecomastia in men.

(ACC/AHA, 2001)

**Dosing:**

Spironolactone. Low doses of 25 mg/day orally.

Amiloride. Initial dose: 5-10 mg daily.

(Combined with other Diuretics) Maximum dose: 20 mg daily. (BNF, 2002)

**Contraindications:**

1- Serious hyperkalaemia, hyponatremia, pregnancy and breast-feeding, Addison’s disease, moderate to severe renal impairment (Spironolactone).

2- Hyperkalaemia and renal failure (Amiloride). (BNF, 2002)

2.6 Angiotensin Receptor Antagonists and Vasodilators (Hydralazine and Nitrates):

Give ARBs if → Intolerance to ACE-Inhibitors due to cough or angioedema. (along with Beta-blockers, Diuretics, and Digoxin).

Give combination of Hydralazine and Isosorbide dinitrate (along with Beta-blockers, Diuretics and Digoxin) if → Intolerance to ACE-Inhibitors due to renal insufficiency.

(ACC/AHA, 2002)

Give combination of Hydralazine and ISDN very cautiously and in low doses if → Intolerance to ACE-Inhibitors due to hypotension. (Consensus panel)

Do not give ARBs to patients taking ACE-Inhibitors and Beta-blockers.

Do not use (or substitute) ARBs or Hydralazine and Nitrates if → ACE-Inhibitors are well-tolerated or not used before.
Consider Beta-blockers before Hydralazine and Nitrates in patients already receiving ACE-Inhibitors.

Do not use Nitrate or Hydralazine alone in treating HF. (ACC/AHA, 2001)

**Dosing of Angiotensin Receptor Antagonists (ARBs), Nitrates and Hydralazine:**

Candesartan: Initial dose: 4 mg once daily (2 mg in renal or hepatic impairment).

   Maintenance dose: 8 mg once daily.

   Maximum dose: 16 mg once daily. (BNF, 2002)

Telmisartan

   Initial dose: 20-40 mg. (Consensus panel)

   Maintenance dose: 40 mg once daily. (Increased if necessary)

   Maximum dose: 80 mg once daily. (BNF, 2002)

Valsartan

   Initial dose: 80 mg once daily (can be 40 mg *).

   Target dose: 160 mg twice daily. (Consensus panel, Cohn et al, 2001)

GTN:

   Oral: longer acting preparations: 5 mg 3 times daily. 10 mg 3 times daily in severe CHF. 5 mg repeated until symptoms abate in acute HF.

Isosorbide dinitrate: Orally: Maintenance dose: 40-160 mg daily, in 2 divided doses.

   Maximum dose: 240 mg.

   iv infusion: 2-10 mg/hour. Maximum: up to 20 mg/hour.

Hydralazine:

   25 mg 3-4 times daily.

   (combined with long acting Nitrates) Increase dose, if necessary, every 2 days.

   (If used alone ➔ tachycardia, fluid retention) Maintenance dose: 50-75 mg 4 times daily. (BNF, 2002)

* Dose should be reduced in elderly > 75 years old, mild to moderate hepatic impairment, moderate to severe renal impairment or intravascular volume depletion, i.e initially 40 mg titrated up to 80 mg.
Use ARBs cautiously in Bilateral renal artery stenosis. (Consensus panel)

**Contraindications:**

1. **ARBs**: Pregnancy, Breast feeding and cholestasis (Candesartan), severe hepatic or renal impairment, biliary obstruction, or breast-feeding (Telmisartan).

2. **Hydralazine**: Idiopathic systemic lupus erythematosus, high output HF, severe tachycardia, dissecting aortic aneurysm, cor pulmonale, porphyria, myocardial insufficiency due to mechanical obstruction.

3. **Nitrates**: Hypotension, hypovolemia, hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis, marked anaemia, head trauma, cerebral haemorrhage, closed-angle glaucoma. (BNF, 2002)

**Treatment in Special Patient Groups:**

a. **Men:**
Do not give Sildenafil (in erectile dysfunction) with Nitrates as it leads to profound hypotension.

b. **HF and Ischemic Heart Diseases (IHD):**
Give drugs appropriate for controlling both IHD and HF, example; ACE-Inhibitors, Beta-blockers, Nitrates.

   In HF and Angina ➔ Give Nitrates and Beta-blockers (with Diuretics and ACE-Inhibitors).

   In HF and history of MI ➔ Give Beta-blockers and ACE-Inhibitors.

   Give antiplatelet drugs for prevention of MI and death.

   If fluid retention occurs ➔ Give Diuretics.

Avoid CCB except Amlodipine.
c- HF and Supraventricular Arrhythmias (most commonly Atrial Fibrillation):

c1 - Control Ventricular Response:
Give Beta-blockers, if ineffective, contraindicated or intolerated ➔ Give Amiodarone, if contraindicated or intolerated ➔ Give Digoxin.

Target rate is a ventricular response: Less than 80-90 bpm, at Rest.

Less than 110-130 bpm, during moderate exercise.

Restoration of sinus rhythm is most warranted in patients with recurrent or sustained atrial arrhythmias, which lead to worsening symptoms.

Avoid antiarrhythmic drugs class I and III (except Amiodarone) such as Dofetilide and Sotalol.
Avoid Verapamil and Diltiazem because they depress the myocardial function.
Consider AV ablation if tachycardia persists despite pharmacological therapy.

c2- Prevent thromboembolic events:
Give Warfarin in HF if ➔
1- Paroxysmal or chronic atrial fibrillation (INR 2.0-3.0).
2- Previous history of thromboembolic events.
3- Markedly depressed EF (< 25%). (ACC/AHA, 2001)
4- Dilated cardiomyopathy.
5- Aneurysm.
6- Advanced LV dilatation (especially if thrombus is detected on echo). (Consensus panel)

Contraindications to Warfarin:
1- Pregnancy. 2- Peptic ulcer. 3- Severe hypertension. 4- Bacterial endocarditis.

Use with caution in patients susceptible to falls, impaired liver function or history of GI bleeding. (BNF, 2002)
d- HF and Ventricular Arrhythmias:

Do every effort to prevent sudden death: through preventing:

1- Acute ischemic events.
2- Bradyarrhythmias.
3- Ventricular arrhythmias. (ACC/AHA, 2001)

If ventricular arrhythmias:

Asymptomatic ➔ Management is left to physician’s discretion. (Consensus Panel)
Symptomatic ➔ Use Beta-blockers, Amiodarone (ACC/AHA, 2001)

Avoid routine use of Amiodarone in HF patients.
Give Amiodarone (alone or in conjunction with Beta-blockers and cardioverter-defibrillator) in patients with history of sudden death, ventricular fibrillation, sustained or unstable ventricular tachycardia.

Avoid class 1A (Quinidine, Procainamide), Class 1C (Flecainide, Ecainide) and some Class III (D-Sotalol) antiarrhythmic drugs because of increased risk of serious arrhythmias, particularly in LVSD.

Drug-use practice for which usefulness or efficacy are less well-established by opinion or evidence (Conflicting evidence and/or divergence of opinion exist, being more not in favour of therapy):
1- Addition of ARBs to ACE-Inhibitors.

2- Addition of Nitrates (alone or with Hydralazine) to ACE-Inhibitors, Diuretics, Beta-blockers and Digitalis in HF only.

3- Anticoagulation in HF patients with no atrial fibrillation (AF) or previous thromboembolic event.

4- Routine use of Amiodarone in asymptomatic ventricular arrhythmias for prevention of sudden death.

5- Restoration of sinus rhythm by electrical cardioversion in HF and AF.
Not recommended drug-use practices: (Evidence and/or agreement that therapy is not useful or ineffective and in some cases maybe harmful):

1- Long term intermittent iv infusion of a positive inotropic drug (Dobutamine, Dopamine, Milrinone).

2- Using ARBs instead of ACE-Inhibitors in patients with HF, who have not been given ACE-Inhibitors or can tolerate therapy.

3- Use of ARBs before a Beta-blocker in HF patients receiving ACE-Inhibitors.

4- Use of antiarrhythmic agents, Class I and III (except Amiodarone), CCB (except Amlodipine and Felodipine), NSAIDs, Tricyclic antidepressants, and corticosteroids.

5- Routine use of nutritional supplements (Coenzyme Q10, carnitine, taurine, and antioxidants) or hormonal therapies (growth hormone, or thyroid hormone) for treatment of HF. (ACC/AHA, 2001)

**Monitoring Therapy:**

1 **Regular evaluation of signs and symptoms:**

1.1 **Signs and symptoms of fluid retention:** LL edema, SOB, PNDs, elevated JVP, etc. (During therapy or up-titration of doses).

1.2 **Blood pressure:** at initiation or up-titration of ACE-Inhibitors and Beta-blockers, particularly if hypovolemia, marked diuresis or severe hyponatremia (Na< 130 mmol/L) exists. Also, when Diuretics are given concomitantly to ACE-Inhibitors, vasodilators, and ARBs.

1.3 **Body weight:** Monitor during Diuretic therapy, patient should not lose more than 0.5-1 kg daily. Also at initiation of Beta-blockers (any increase in weight should be treated by increasing dose of Diuretic to restore weight to pre-treatment levels).
1.4 Electrolytes: Monitor serum Potassium:

a- Within 1-2 weeks of ACE-Inhibitor initiation, then periodically thereafter. Especially in patients receiving Potassium supplements, have impaired renal function, or taking Potassium-sparing diuretics, particularly if DM co-exists.

b- During ARBs therapy, particularly in elderly, renal impairment, a lower initial dose maybe appropriate in these patients. (BNF, 2002; ACC/AHA, 2001)

c- Concomitant treatment with ACE-Inhibitors and Spironolactone,

d- Spironolactone therapy especially in impaired renal function. Serum Potassium levels should be < 5 mmol/L, and creatinine < 2.5 mg/dl before starting Spironolactone.

e- Combination of Diuretics: Loop Diuretics and Metolazone.

Monitor serum Potassium and Magnesium levels, particularly in patients on Digoxin (hypokalemia precipitates Digitalis toxicity), or combination of Diuretics. Maintain K level at 3.8- 5.1 mmol/L.

1.5 Renal function: Serum creatinine and BUN

- Mild to moderate degrees of functional impairment  Changes in BUN and serum creatinine are usually insignificant and do not require withdrawing drugs.

- Serum creatinine:
  - > 3 mg/dl  Increased toxicity of established treatment  Adjust doses.
  - > 5 mg/dl  Hemofiltration or dialysis.

Monitor renal function (BUN and serum creatinine) with:

1- High dose of Diuretics (precipitate azotemia).

2- ACE-Inhibitors especially in:
  1- Pre-existing hypotension.
  2- Pre-existing hyponatremia.
  3- DM.
  4- Azotemia. (ACE-Inhibitors increase BUN).

3- Diuretics concomitantly given with ACE-Inhibitor, ARBs and vasodilators.

4- Spironolactone therapy and ARBs because they can cause hyperkalaemia and worsen renal function. (ACC/AHA, 2001)
1.6 Digoxin Therapy:
Do not use serum Digoxin levels to guide selection of doses. Serum levels are used to assess toxicity and not efficacy of the drug.

**Digoxin Toxicity:**
Usually associated with serum levels (>2 ng/dl), if suspected measure serum level.

A- **Signs:**
1. Cardiac arrhythmias (heart block, ectopic and re-entrant cardiac rhythm).
2. GI symptoms (nausea, vomiting, anorexia).
3. Neurological complaint (visual disturbances, disorientation, confusion).

B- **Precipitating factors:**
1. Hypokalemia, hypomagnesaemia and hypothyroidism.
2. Concomitant use of Quinidine, Spironolactone, Flecanide, Verapamil, Propafenone, and Amiodarone.

**Management of Refractory End-stage HF:**
Once accurate diagnosis of refractory HF, is confirmed 1- Identify contributing factors.

- Ensure optimum conventional therapy.

Consider special treatment strategies: 1- Mechanical circulatory support.

- Continuous positive inotropic agents.
- Cardiac transplantation.

1. Restrict dietary Sodium intake (2 g daily or less).
2. Identify and control fluid retention.
   - If resistant edema ➔ Increase Loop Diuretic dose or add another Diuretic, example: Metolazone.
   - If volume overload continues give iv Diuretics, either alone or in conjunction with Dopamine and Dobutamine.
   - If renal dysfunction is severe or edema is resistant to therapy ➔ Ultra-filtration or hemo-filtration.
   - Consider Spironolactone, particularly with reserved renal function. Monitor Potassium levels especially in impaired renal function.
• Do not discharge from hospital until a stable and effective Diuretic regimen is established.

3- Palliation of symptoms and stabilization of patients through continuous infusion of both positive inotropic agents (Dopamine, Dobutamine, or Milrinone) and vasodilator drugs (Nitroglycerine, Nitroprusside). Once clinical stability is achieved shift to oral regimen.

4- Give ACE-Inhibitors and Beta-blockers, and monitor BP, renal function, and signs and symptoms of HF.
• ACE-Inhibitors and Beta-blockers should not be initiated if: SBP< 80 mmHg (signs of hypoperfusion).
• Do not start Beta-blockers if: - Significant fluid retention exists.
• Intravenous positive inotropic agent was recently required.
• If ACE-Inhibitors are intol erated then give ARBs.
• If ACE-Inhibitors or Beta-blockers are not tolerated, then give Nitrates and Hydralazine.

5- Assess patient for at least 48 hours in hospital, after shifting to oral regimen to assess adequacy of therapy.

6- Follow other measures recommended in HF patients with stage C.

7- Avoid using routine intermittent infusion of positive inotropic agents.

(ACC/AHA, 2001)

Dosing of Inotropic sympathomimetic (positive inotropic agents):

Dobutamine: iv infusion 2.5-10 microgram/kg/minute. Adjusted according to response.
Dopamine: iv infusion 2-5 microgram/kg/minute. Adjusted according to dose. Doses > 5 microgram/kg/minute result in vasoconstriction and exacerbate HF.
Contraindications to Inotropic Sympathomimetics:

1- Tachyarrhythmias and Phaeochromocytoma (Dopamine).

2- No contraindications were stated for Dobutamine, however, tachycardia and marked increase in SBP was stated to indicate overdose. (BNF, 2002)
References:


ACC Website. Available at: www.acc.org/clinical/guidelines/failure/hf_index.htm


*The most up-to-date guidelines on management of HF, available from ACC/AHA.
11: Letters of Cardiologists’ Approval of the Templates.
Re: Cardiovascular Drug Utilization in IHD and HF Patients at Jordanian Hospitals.

To whom it may concern,

I confirm that I have been involved in the above research project as co investigator. The research has required the development of guidelines for the clinical management of IHD (stable angina, unstable angina, and myocardial infarction) and HF. I confirm that these templates have been reviewed and validated by myself and other Jordanian cardiologists, and they are approved for clinical use at Jordanian hospitals. The templates will require updating as necessary to remain of valid application.

If you have any queries, please do not hesitate to contact me.

Kind regards,

Dr name: ..............................

Signature: ..............................

E-mail: ..............................

Date: ..............................
Re: Cardiovascular Drug Utilization in IHD and HF Patients at Jordanian Hospitals.

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If you have any queries, please do not hesitate to contact me.

Kind regards,

Dr name: ...N. A. KADRI, M.D, FACC...
Signature: ...
E-mail: n.kadri@sencon.com.jo...
Date: 13th of Sept. 2020.

Tel: 962-6-5680060 / Telefax 962-6-5680061 / P.O Box 941164- Shmesani, 11194 Amman - Jordan
Re: Cardiovascular Drug Utilization in IHD and HF Patients at Jordanian Hospitals.

To whom it may concern,

I confirm that I have been involved in the above research project as co-investigator. The research has required the development of guidelines for the clinical management of IHD (stable angina, unstable angina, and myocardial infarction) and HF. I confirm that these templates have been reviewed and validated by myself and other Jordanian cardiologists, and they are approved for clinical use at Jordanian hospitals. The templates will require updating as necessary to remain of valid application.

If you have any queries, please do not hesitate to contact me.

Kind regards,

Dr name: Ahmad H. Assonah

Signature: _____________________________

Address: P.O Box 4141 - 1118 - Jordan

E-mail: hassonah@doctors.net.uk

Date: _____________________________

A) Sample of Case Vignettes:

**Patient code:** 221  
**Age:** 40 years old  
**Gender:** Male  
**Ward:** Medical  
**Length of follow up:** 2 days.  
**Weight:** not documented.

**HPC:** left shoulder and arm pain for 3 days.

**PMH:** HTN DM

**Allergies:** nothing documented.

**DHx:** oral hypoglycaemic agents.

**SHx:** nothing documented.  
**FHx:** positive family history of IHD.

**O/E:** BP 120/80 mmHg  
Temp: 36.2 C

**Diagnosis:** Unstable angina

**Medication on Admission and Second day hospitalization:**
- GTN 5 mg x 1 (Nitroderm TTS)
- Aspirin 1 tablet x 1 (dose not documented, brand = Bufferin)
- Enoxaparin 80 mg SC x 2
- Prendopril 2 mg PO x 1

**Laboratory Investigations:**

**First day:**
- Na, K, Cl, Urea, Creatinine = normal.
- Uric acid = 8.8 mg/dl (3-7)
- FBS = 12.7 mg/dl (4.1-9.4)
- AST = 43 U/l (<37)
- LDH, CPK = normal
- WBC = 10.3 (4.5-10)
- RBC, Hgb, platelets = normal.

**Second day:**
- FBS = 12.1 mg/dl (4.1-9.4)
- HDL = 32 mg/dl (35-55)
- LDL = 118 mg/dl (< 130)
- TG = 293 mg/dl (50-150)
- VLDL = 59 mg/dl (6-40)
- Cholesterol = 209 mg/dl (200-239)
- Albumin = 3.7 gm/dl (3.5-5.4)

**Follow Up of patients:**

**Second day:**
- ECG = normal heart size, good left ventricular systolic and diastolic functions.
- EF = 70%, Normal valves.
B) Checklists for the Evaluation of CHD and HF Therapy:

**Checklist for Stable Angina**

<table>
<thead>
<tr>
<th>DUE criteria</th>
<th>Researcher's Comments</th>
<th>Validator's comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is Aspirin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If no, is an alternative prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a b-blocker prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent was chosen? (Circle)</td>
<td>Propranolol - Metoprolol - Atenolol - Pindolol - Bisoprolol - Aecbutolol - Others</td>
<td></td>
</tr>
<tr>
<td>Is an ACE-Inhibitor prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent was chosen? (Circle)</td>
<td>Captopril - Enalapril - Lisinopril - Ramipril - Fosinopril - Other</td>
<td></td>
</tr>
<tr>
<td>Are Nitrates given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agents?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a CCB prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent was chosen? (Circle)</td>
<td>Verapamil - Diltiazem - Amlodipine - Others</td>
<td></td>
</tr>
<tr>
<td>Drug use Criteria</td>
<td>Researcher’s comments</td>
<td>Validator’s comments</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
<td>-----------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Is Lipid-lowering drug given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent was chosen? (Circle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins - Fibrates - Nicotinic Acid - Bile Acid sequestrants. Specify:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the patient prescribed any of the following:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimetazidine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Warfarin?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Hirudin?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>LMWH?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Short acting, immediate release dihydropyridines , i.e Nifedipine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Dipyridamole?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>GP IIb/IIIa antagonists?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
2. **Therapy Monitoring:**

<table>
<thead>
<tr>
<th>Therapy Monitoring Criteria</th>
<th>Yes / No</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is ischemic pain monitored?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the following monitored:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Blood pressure?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Heart rate (target 55-60 bpm at rest)?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Renal function: before starting ACE-Inhibitors?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Urea</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Creatinine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Fasting lipid Profile (LDL, HDL, TG, total cholesterol)?</td>
<td></td>
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<td></td>
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<tr>
<td>- Liver transaminases (during statin therapy)?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. **Follow up of Patients:**

<table>
<thead>
<tr>
<th>Follow-up Aspects</th>
<th>Researcher’s Comments</th>
<th>Validator’s Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is ischemic pain followed up?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is BP and HR followed up?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**List of Contraindications:**

<table>
<thead>
<tr>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B-blockers:</strong> severe bradycardia, marked first degree AV block, any second or third AV block, sick sinus syndrome, severe unstable HF, cardiogenic shock, asthma and bronchospastic disease, severe depression, severe peripheral vascular disease with rest ischemia, hypotension.</td>
</tr>
<tr>
<td><strong>ACE-Inhibitors:</strong> Angioedema, Anuric renal failure, Bilateral renal artery stenosis.</td>
</tr>
<tr>
<td><strong>CCB:</strong> heart failure (except with Amlodipine and Felodipine), Bradycardia, sinus node dysfunction, and AV nodal block (with Verapamil or Diltiazem), Long QT interval (with Bepridil).</td>
</tr>
<tr>
<td><strong>Nitrates:</strong> hypertrophic obstructive cardiomyopathy, severe aortic valve stenosis.</td>
</tr>
<tr>
<td><strong>Aspirin:</strong> allergy, active bleeding, active retinal bleeding, active peptic ulcer, hemophilia and other serious sources of gastrointestinal or genitourinary bleeding.</td>
</tr>
<tr>
<td><strong>Statins:</strong> active or chronic liver disease.</td>
</tr>
<tr>
<td><strong>Fibrates:</strong> Severe hepatic or renal insufficiency.</td>
</tr>
<tr>
<td><strong>Bile acid sequestrants:</strong> TG &gt; 400 mg/dl, Familial dysbeta-lipoproteinemia.</td>
</tr>
<tr>
<td><strong>Nicotinic acid:</strong> chronic liver disease, severe gout.</td>
</tr>
</tbody>
</table>
4. Drug Dosing:

<table>
<thead>
<tr>
<th>Daily dose</th>
<th>Within range</th>
<th>Researcher's comments</th>
<th>Validator's comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin 75 - 325 mg x 1</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Clopidogrel 75 mg x 1</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine 250 mg x 2</td>
<td></td>
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<tr>
<td>Captopril 25 mg x 2-3 (max 150 mg)</td>
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<tr>
<td>Ramipril ID 2.5 mg x 1 for 1 week, then 5 mg x 1 for 3 weeks, MD 10 mg x 1</td>
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</tr>
<tr>
<td>Lisinopril MD 10 mg x 1 (SBP &gt;120 mmHg) MD 5 mg x 1 (SBP = 100-120 mmHg)</td>
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</tr>
<tr>
<td>Enalapril ID 2.5 mg x 1, MD 20 mg x 1 in 1-2 doses</td>
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</tr>
<tr>
<td>Propranolol PO 20-80 mg x 2</td>
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<td></td>
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<tr>
<td>Metoprolol PO 50-200 mg x 2</td>
<td></td>
<td></td>
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<tr>
<td>Atenolol PO 50-200 mg x 1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Acebutolol PO 200-600 mg x 2</td>
<td></td>
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</tr>
<tr>
<td>Bisoprolol PO 10-20 mg x 1</td>
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<tr>
<td>Pindolol PO 2.5 - 7.5 mg x 3</td>
<td></td>
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</tr>
<tr>
<td>Amlodipine PO 5 -10 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Verapamil PO IR 80-160 mg x 3 SR 120-480 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem PO ImR 30-60 mg x 3 InR 90-120 mg x 2 SR 200-300 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTN SL 0.3-0.6 mg (max 1.5 mg) iv 5-200 mcg/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISDN PO 5-80 mg x 2-3 iv 1.25 - 5 mg/h</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Simvastatin PO 20-80 mg x 1, Max 10 mg if combined with fibrates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvastatin PO 20-80 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin PO 20-80 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrovastatin PO 10-80 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gemfibrozil PO 600 mg x 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimetazidine PO 20 mg x 3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Checklist for UA/NSTEMI

#### 1. Choice of Drugs:

<table>
<thead>
<tr>
<th>Drug choice Criteria</th>
<th>Researcher's Comments</th>
<th>Validator's Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is Aspirin prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>If No, is an alternative prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is GTN SL prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is iv GTN prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>If yes, how long is GTN iv infusion?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is an oral ISDN prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is Morphine sulfate prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is Metoclopramide or Cyclizine prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is an iv b-blocker prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is an oral b-blocker prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent is used? (Circle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol - Metoprolol - Atenolol - Acebutolol* - Pindolol* - Labetolol.*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
</tbody>
</table>

* Agents with intrinsic sympathomimetic activity are less preferable than other b-blockers.
<table>
<thead>
<tr>
<th>Drug Choice Criteria</th>
<th>Researcher's Comments</th>
<th>Validator's Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is an ACE-Inhibitor prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent is used?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a CCB prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent is used (Circle): Diltiazem, Verapamil, Nifedipine, others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Clopidogrel/ Ticlopidine added to Aspirin?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>If CABG is scheduled, is Clopidogrel withheld 5-7 days before it?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is heparin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it prescribed for 2-5 days?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a LMWH prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If PCI scheduled, which is prescribed: (Circle)</td>
<td>Heparin or Enoxaparin</td>
<td></td>
</tr>
<tr>
<td>If CABG scheduled, which is prescribed: (Circle)</td>
<td>Heparin or Enoxaparin</td>
<td></td>
</tr>
<tr>
<td>Drug choice criteria</td>
<td>Researcher’s comments</td>
<td>Validator’s comments</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Is a GP IIb/IIIa antagonist prescribed? Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct? Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which agent is used? (Circle) Abciximab, Tirofiban, Eptifibatide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a lipid lowering agent prescribed? Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct? Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Which agent is prescribed? (Circle):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statins - Fibrates - Nicotinic Acid - Bile acid sequestrants. Specify _______</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is any of the following prescribed?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Nitrates with Sildenafil Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Short acting, immediate-release dihydropyridines. With b-blockers - without b-blockers Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Thrombolytic therapy. Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Abciximab if PCI is not planned. Yes No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Dipyridamole, Sulfinpyrazone, Prostacyclin. Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Eptifibatide or Tirofiban (added to aspirin, LMWH or UFH in the absence of continuing ischemia or PCI) Yes No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2. Monitoring Therapy:

<table>
<thead>
<tr>
<th>Aspects of monitoring therapy</th>
<th>Researcher’s Comments</th>
<th>Validator’s Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is ischemic pain monitored?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is BP monitored before and during treatment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is heart rate monitored (before and during b-blocker therapy)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is fasting lipid profile done (LDL, TG, HDL, total cholesterol)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic transaminases during statins therapy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is renal function (creatinine and urea) monitored?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is PTT monitored to reach 1.5-2.5 times control? At 6 hours from starting heparin or every dose change, then every 24 hrs after reaching therapeutic level.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, hematocrit, platelet count daily during heparin therapy?</td>
<td></td>
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<tr>
<td>Hemoglobin, platelet count on daily basis during GP IIb/IIIa antagonist treatment?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets and white cells count during Ticlopidine therapy?</td>
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<td></td>
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</tbody>
</table>

3. Follow-up of Patients:

<table>
<thead>
<tr>
<th>Follow-up Aspects</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is ischemic pain relieved?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is BP controlled?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is anticoagulation therapy followed up?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whether signs of bleeding exist or not?</td>
<td></td>
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</table>
List of Contraindications:

<table>
<thead>
<tr>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-blockers</strong>: severe bradycardia, marked first degree AV block, any second or third degree AV block in absence of pace-maker, sick sinus syndrome, severe unstable HF, Asthma and bronchospastic disease, severe depression, severe peripheral vascular disease with rest ischemia.</td>
</tr>
<tr>
<td><strong>ACE-Inhibitors</strong>: Angioedema, Anuric renal failure, Bilateral renal artery stenosis.</td>
</tr>
<tr>
<td><strong>CCB</strong>: heart failure (except with Amlodipine and Felodipine), Bradycardia, sinus node dysfunction, and AV nodal block, pulmonary edema or severe LV dysfunction (with Verapamil or Diltiazem), Long QT interval (with Bepridil).</td>
</tr>
<tr>
<td><strong>Nitrates</strong>: hypertrophic obstructive cardiomyopathy, severe aortic valve stenosis.</td>
</tr>
<tr>
<td><strong>Aspirin</strong>: allergy, active bleeding, active retinal bleeding, active peptic ulcer, hemophilia and other serious sources of gastrointestinal or genitourinary bleeding.</td>
</tr>
<tr>
<td><strong>Statins</strong>: active or chronic liver disease.</td>
</tr>
<tr>
<td><strong>Fibrates</strong>: Severe hepatic or renal insufficiency.</td>
</tr>
<tr>
<td><strong>Bile acid sequestrants</strong>: TG &gt; 400 mg/dl, Familial dysbeta-lipoproteinemia.</td>
</tr>
<tr>
<td><strong>Nicotinic acid</strong>: chronic liver disease, severe gout.</td>
</tr>
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</table>
4. Drug Dosing:

<table>
<thead>
<tr>
<th>Daily dose</th>
<th>within range</th>
<th>Researcher's comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin ID 160-325 mg x 1, MD 75-160 mg x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel PO 75 mg x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>Ticlopidine PO 250 mg x 2</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTN SL 0.3- 0.6 mg (up to 1.5 mg)</td>
<td>Yes/No</td>
<td></td>
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</tr>
<tr>
<td>Spray 0.4 mg</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>iv 5-200 mcg/min</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical 5, 10 patch/day, max 10 x 2</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>ISDN SL 5-10 mg, PO 5-80 mg x 2-3</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>Morphine sulphate 1-5 mg iv, repeat PRN every 5-30 min</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide 10 mg x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine 50 mg iv x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>Metoprolol iv 5 mg x 3 (up to 15 mg)</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>PO ID 25-50 mg Q 6 hrs for 48 hrs</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>MD 50-200 mg x 2</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol iv 0.5-1 mg</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>PO 20-80 mg x 2</td>
<td>Yes/No</td>
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<tr>
<td>Atenolol iv 5 mg x 2 (after 5 min)</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>PO 50-200 mg x 1</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>Bisoprolol PO 10-20 mg x 1</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>Amlodipine PO 5-10 mg x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>Felodipine PO 5-10 mg x 1</td>
<td>Yes/No</td>
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<tr>
<td>Verapamil IR 80-160 mg x 3</td>
<td>Yes/No</td>
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<tr>
<td>SR 120-480 mg x 1</td>
<td>Yes/No</td>
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<tr>
<td>Diltiazem ImR 30-60 mg x 3</td>
<td>Yes/No</td>
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<tr>
<td>InR 90-120 mg x 2</td>
<td>Yes/No</td>
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<tr>
<td>SR 200-300 mg x 1</td>
<td>Yes/No</td>
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<td></td>
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<tr>
<td>Captopril Initial PO 6.25 mg</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>MD max 150 mg divided doses</td>
<td>Yes/No</td>
<td></td>
<td></td>
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<tr>
<td>Enalapril ID 2.5 mg x 1, MD 10 mg x 1-2</td>
<td>Yes/No</td>
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<tr>
<td>Ramipril ID PO 2.5 mg x 1 for 1 week, then 5 mg x 1 for 3 weeks, MD 10 mg x 1</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Yes/No</td>
<td></td>
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<tr>
<td>MD 10 mg x 1 (SBP &gt;120 mmHg)</td>
<td>Yes/No</td>
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<tr>
<td>MD 5 mg x 1 (SBP = 100-120 mmHg)</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily Dose</td>
<td>within range</td>
<td>Researcher's Comments</td>
<td>Validator's Comments</td>
</tr>
<tr>
<td>----------------------------</td>
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</tr>
<tr>
<td>Heparin</td>
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<tr>
<td>iv bolus 60-70 U/Kg (max 5000 U)</td>
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<tr>
<td>iv infusion: 12-15 U/kg/hr (max 1000 U/hr) for 2-5 days</td>
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<tr>
<td>Enoxaparin 1 mg/kg SC Q 12 hrs</td>
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<tr>
<td>Dalteparin 120 IU/kg SC Q 12 hrs</td>
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<tr>
<td>Abciximab 0.25 mg/kg bolus, iv infusion 0.125 mcg/kg/min (max 10 mcg/kg/min) for 12 to 24 hrs.</td>
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<tr>
<td>Eptifibatide 180 mcg/kg bolus, infusion 2 mcg/kg/min for 72-96 hrs</td>
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<tr>
<td>Tirofiban 0.4 mcg/kg/min for 30 min, then infusion 0.1 mcg/kg/min for 48 to 96 hrs</td>
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<tr>
<td>Simvastatin PO 20-80 mg x 1 (max 10 mg if combined with fibrates)</td>
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<tr>
<td>Pravastatin PO 20-80 mg x 1</td>
<td></td>
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<tr>
<td>Fluvastatin PO 20-80 mg x 1</td>
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<tr>
<td>Atrovastatin PO 10-80 mg x 1</td>
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<tr>
<td>Gemfibrozil PO 600 mg x 2</td>
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<tr>
<td>Clofibrate PO 1000 mg x 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimetazidine PO 20 x 3*</td>
<td></td>
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</tbody>
</table>

* Consensus panel.
### Checklist for MI

**Choice of Therapy:**

<table>
<thead>
<tr>
<th>Drug choice criteria</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute phase (0-24 hrs):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is Aspirin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is morphine sulfate prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Metoclopramide or Cyclizine prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a fibrinolytic prescribed (&lt;12 hrs)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is heparin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it continued for 24-48 hours post MI?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a LMWH prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a GP IIb/IIIa inhibitor given with fibrinolitics?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is an iv B-blocker prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is an oral b-blocker prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is an ACE-Inhibitor prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Drug Choice Criteria</td>
<td>Researcher's comments</td>
<td>Validator's comments</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Are Nitrates prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is a CCB prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td><strong>Post Acute Phase:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is Aspirin continued?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is a b-blocker continued?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is an ACE-Inhibitor continued?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent used?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a CCB prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is a lipid lowering drug given?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is Clopidogrel prescribed?</td>
<td>Yes  No</td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes  No</td>
<td></td>
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</tbody>
</table>
### Drug choice Criteria

<table>
<thead>
<tr>
<th>Drug choice Criteria</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is Warfarin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Heparin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a LMWH prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are nitrates prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Is Lidocaine prescribed in the absence of ventricular arrhythmia (VF)? | Yes | No |

### 2. Monitoring therapy:

<table>
<thead>
<tr>
<th>Monitoring therapy criteria</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the following monitored:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Ischemic pain?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Blood pressure?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Heart rate?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Renal function before ACE-Inhibitor initiation?</td>
<td>Urea</td>
<td>Creatinine</td>
</tr>
<tr>
<td>- PTT at 3, 6, 12, 24 hrs after starting heparin, also upon dose change, then daily after reaching a therapeutic PTT? (1.5-2.5 times control, 70 sec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Fasting lipid profile? (LDL, HDL, TG, total cholesterol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Liver transaminases during statin therapy?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3. Follow up of Patients:

<table>
<thead>
<tr>
<th>Follow up aspect</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is ischemic pain relieved?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are blood pressure and heart rate followed up?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is patient followed up for any signs of bleeding?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**List of Contraindications**

**Contraindications**

- **B-blockers**: severe bradycardia, marked first degree AV block, any second or third degree AV block in absence of pace-maker, sick sinus syndrome, severe unstable HF, cardiogenic shock, Asthma and bronchospastic disease, severe depression, severe peripheral vascular disease with rest ischemia, hypotension.

- **ACE-Inhibitors**: Angioedema, Anuric renal failure, Bilateral renal artery stenosis.

- **CCB**: heart failure (except with Amlodipine and Felodipine), Bradycardia, sinus node dysfunction, and AV nodal block, pulmonary edema or severe LV dysfunction (with Verapamil or Diltiazem), Long QT interval (with Bepridil).

- **Nitrates**: hypertrophic obstructive cardiomyopathy, severe aortic valve stenosis.

- **Aspirin**: allergy, active bleeding, active retinal bleeding, active peptic ulcer, hemophilia and other serious sources of gastrointestinal or genitourinary bleeding.

- **Statins**: active or chronic liver disease.

- **Fibrates**: Severe hepatic or renal insufficiency.

- **Bile acid sequesterants**: TG > 400 mg/dl, Familial dysbeta-lipoproteinemia.

- **Nicotinic acid**: chronic liver disease, severe gout.
4. **Drug Dosing:**

<table>
<thead>
<tr>
<th>Daily dose</th>
<th>Within range</th>
<th>Researcher's comments</th>
<th>Validator's comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine: iv inj 4-8 mg (2-5 mg in elderly + frail). Additional 2 mg at 5 min interval till pain relieved</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diamorphine iv inj 5 mg, (reduce dose in elderly + frail). Additional 2.5-5 mg PRN.</td>
<td>Yes/No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide iv inj 10 mg x 1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cyclizine iv inj 50 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Aspirin PO 150-325 mg x 1 chewable or dispensed in water</td>
<td></td>
<td></td>
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<tr>
<td>Clopidogrel PO 75 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Streptokinase 1.5 million units in 100 ml NS or dextrose over 30-60 min</td>
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</tr>
<tr>
<td>Alteplase iv bolus 15 mg, 0.75 mg/kg over 30 min, 0.5 mg/kg over 60 min, Max dose: 100 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenecteplase: 30 mg if &lt; 60 kg 35 mg if 60 to &lt; 70 kg 40 mg if 70 to &lt; 80 kg 45 mg if 80 to &lt; 90 kg 50 mg if &gt; or = 90 kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin: iv bolus 60 U/kg, max 4000 U. iv infusion: 12-15 U/kg, max 1000 U/hr for 24-48 hours</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Enoxaparin SC bolus 30 mg, followed by SC inj 1 mg/kg Q 12 hrs, for max 7 days</td>
<td></td>
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<tr>
<td>Dobutamine iv infusion 2-15 mcg/kg/min</td>
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</tr>
<tr>
<td>Atenolol iv inj 5 mg over 5 min, PO 50 mg after 5-10 min, 50 mg after 12 hrs. MD 100 mg x 1</td>
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<td></td>
</tr>
<tr>
<td>Metoprolol iv inj 5 mg Q 2 min (max 15 mg), then after 15 min PO 50 mg x 4 for 2 days, MD 200 mg in divided doses</td>
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<td></td>
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<tr>
<td>GTN iv infusion 10-200 mcg/min</td>
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<tr>
<td>ISDN iv infusion 2-10 mg/hr up to 20 mg/hr</td>
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<td></td>
</tr>
<tr>
<td>Atropine (bradycardia, heart block) 0.6-1 mg iv bolus up to 2 mg (0.4 mg/kg).</td>
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</tr>
<tr>
<td>Captopril PO ID 6.25 mg x 1, up to 150 mg x 1 in divided doses.</td>
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</tr>
<tr>
<td>Lisinopril PO ID 5 mg x 1 for 2 days, then MD 10 mg x 1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril PO ID 2.5 mg x 1, MD 5-20 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily dose</td>
<td>within range</td>
<td>Researcher’s comments</td>
<td>Validator’s comments</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------</td>
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</tr>
<tr>
<td><strong>Ramipril PO ID 2.5 mg x 2 (2 days), MD 2.5-5 mg x 2</strong></td>
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</tr>
<tr>
<td><strong>Post Infarction phase:</strong></td>
<td></td>
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</tr>
<tr>
<td>Aspirin PO 75-325 mg x 1</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Clopidogrel PO 75 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Propranolol PO 40 mg x 4 for 2-3 days, MD 80 mg x 2</td>
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<tr>
<td>Metoprolol PO 200 mg in divided doses</td>
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<td></td>
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<tr>
<td>Atenolol PO 100 mg in 1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carvedilol PO ID 6.25 mg x 2, MD 25 mg x 2 (max dose increased over 4-6 weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE-Inhibitors: doses stated above</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem PO 300 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Verapamil PO 120 mg x 2-3</td>
<td></td>
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</tr>
<tr>
<td>ISDN PO 5-80 mg x 2-3, SL 5-10 mg PRN</td>
<td></td>
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</tr>
<tr>
<td>Simvastatin ID: 20 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max dose: 80 mg x 1 (10 mg x 1 if combined with fibrates, nicotinic acid or Ciclosporine)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pravastatin ID 20 mg x 1, Max dose: 80 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrovastatin ID 20 mg x 1, Max dose: 80 mg x 1</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

ID initial dose, SC subcutaneous, MD: maintenance dose, Max dose: maximum dose, inj: injection, PO: orally
### Checklists for HF

#### 1. Choice of Drugs:

<table>
<thead>
<tr>
<th>Drug choice criteria</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is a diuretic prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is diuretic continued even after resolution of fluid retention?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is an ACE-Inhibitor prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent? (Circle) Captopril, Enalapril, Lisinopril, Ramipril, Others</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a β-blocker prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Digoxin prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Digoxin used as a primary therapy in decompensating HF?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Spironolactone prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a potassium supplement prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is an Angiotensin receptor antagonist prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Drug choice Criteria</td>
<td>Researcher's comments</td>
<td>Validator's comments</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Is an Angiotensin receptor II antagonist given with ACE-Inhibitor and b-blocker?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it given prior to or instead of well-tolerated ACE-Inhibitors?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a nitrate prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is Hydralazine prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are either nitrate or Hydralazine being prescribed alone?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is CCB prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Which agent?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is a direct-vasodilator prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>In Management of Supraventricular Arrhythmia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is b-blocker prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Amiodarone prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Are any antiarrhythmic class I or III given i.e Satolol, Dofetilde?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Verapamil or Diltiazem given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Warfarin given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Drug choice criteria</td>
<td>Researcher's comments</td>
<td>Validator's comments</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
<td>-----------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td><strong>Ventricular arrhythmia:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is a b-blocker given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Amiodarone given?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is it correct?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is Amiodarone prescribed in asymptomatic VA?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is any of Class IA (Quinidine, Procainamide), Class IC (Flecainide, Ecainide) and Class III (D-Sotalol) prescribed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is patient given long term intermittent infusion of any of the following:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Dobutamine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Is the patient prescribed NSAIDs (anti-inflammatory dose), Tricyclic antidepressant or Corticosteroids?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
2. **Therapy Monitoring:**

<table>
<thead>
<tr>
<th>Therapy Monitoring Criteria:</th>
<th>Researcher's comments</th>
<th>Validator's comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the following Monitored:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Weight?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Signs of edema?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Heart rate?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Renal function: Creatinine?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>BUN?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Electrolytes: Potassium (K)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sodium (Na)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Magnesium (Mg)?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>INR (if warfarin is given)?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

3. **Follow-up of Patients:**

<table>
<thead>
<tr>
<th>Follow-up Aspects</th>
<th>Researcher's comments</th>
<th>Validator's comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms of edema, SOB, PND's, elevated JVP, Weight.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP, HR, Arrhythmias</td>
<td></td>
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</tr>
<tr>
<td>If signs and symptoms of Digoxin toxicity ==&gt; is Digoxin level measured? Is sampling time recorded?</td>
<td></td>
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</tr>
</tbody>
</table>
4. **Drug dosing:**

<table>
<thead>
<tr>
<th>Daily dose</th>
<th>Within range</th>
<th>Researcher’s comments</th>
<th>Validator’s comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frusemide</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PO ID: 20-40 mg x 1-2</td>
<td></td>
<td></td>
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<tr>
<td>MD: 20 mg x 1, or 40 mg on alternate days. 80 mg in resistant edema.</td>
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<tr>
<td>iv injection: 20-50 mg</td>
<td></td>
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<tr>
<td>iv infusion: rate not exceeding 4 mg/min.</td>
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<tr>
<td>Captopril ID: 6.25-12.5 mg x 1</td>
<td></td>
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<tr>
<td>MD: 25 mg x 2-3, TD: 50 mg x 3</td>
<td></td>
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<tr>
<td>Enalapril ID: 2.5 mg x 1</td>
<td></td>
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<tr>
<td>MD: 10 mg x 1-2, TD: 20 mg x 2</td>
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<tr>
<td>Lisinopril ID: 2.5 mg x 1</td>
<td></td>
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<tr>
<td>MD: 5-20 mg x 1, TD: 40 mg x 1</td>
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</tr>
<tr>
<td>Fosinopril: ID: 10 mg x 1</td>
<td></td>
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<tr>
<td>TD: 40 mg x 1</td>
<td></td>
<td></td>
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<tr>
<td>Ramipril: ID 1.25-2.5 mg x 1</td>
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<tr>
<td>TD: 10 mg x 1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Carvedilol: ID 3.125 mg x 2, increased at 2 week interval to 6.25 mg x 2, then 12.5 mg x 2, then 25 mg x 2</td>
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<tr>
<td>Max dose: 25 mg x 2 (&lt; 85 kg)</td>
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<tr>
<td>50 mg x 2 (&gt;85 kg)</td>
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<tr>
<td>Metoprolol Tartarate:</td>
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<tr>
<td>ID: 6.25 mg x 2, Max dose: 75 mg x 2</td>
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<tr>
<td>Metoprolol Succinate (SR)</td>
<td></td>
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<tr>
<td>ID: 12.5 -25 mg x 1, Max dose: 200 mg x 1</td>
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<tr>
<td>Bisoprolol:</td>
<td></td>
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<tr>
<td>ID 1.25 mg x 1, for 1 week, then up-titration over 6 weeks.</td>
<td></td>
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</tr>
<tr>
<td>MD: 10 mg x 1, Max dose: 10 mg x 1</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Digoxin: 0.125 - 0.25 mg x 1</td>
<td></td>
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<tr>
<td>No need for a loading dose</td>
<td></td>
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<tr>
<td>Spironolactone 25 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Amiloride ID: 5-10 mg x 1, MD: 20 mg x 1</td>
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<tr>
<td>Valsartan: ID: 40 - 80 mg x 1</td>
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<tr>
<td>TD: 160 mg x 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan: ID 4 mg x 1 (2 mg in hepatic or renal impairment)</td>
<td></td>
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<td></td>
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<tr>
<td>MD: 8 mg x 1</td>
<td></td>
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</tr>
<tr>
<td>Max dose: 16 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily dose</td>
<td>Within Range</td>
<td>Researcher’s comments</td>
<td>Validator’s comments</td>
</tr>
<tr>
<td>------------</td>
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<td>-----------------------</td>
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</tr>
</tbody>
</table>
| Telmisartan: ID: 20-40 mg x 1  
MD: 40 mg x 1  
Max dose: 80 mg x 1 | | | |
| ISDN: PO MD: 20-80 mg x 2  
Max dose: 240 mg daily.  
iv infusion: 2-10 mg/hr, max up to 20 mg/hr. | | | |
| Hydralazine: 25 mg x 3-4  
MD: 50-75 mg x 4 | | | |
| Warfarin according to INR in AF, INR (2.0-3.0) | | | |
| Amiodarone MD: 200 mg PO, or minimum dose to control arrhythmia. | | | |
| Dopamine: iv infusion: 2-5 mcg/kg/min, adjust according to response. | | | |
| Dobutamine: iv infusion: 2.5-10 mcg/kg/min, adjust according to response. | | | |

* Only 4 out of 6 templates are shown. The remaining two templates for the assessment of therapy in SA/HF and UA/HF patients comprise the same DUE criteria listed in above the SA, HF templates and the UA, HF templates, respectively.*
THE END