A COST EVALUATION ANALYSIS TO IDENTIFY SOLUTIONS FOR AFFORDABLE MEDICINES IN JORDAN- A COMPARATIVE STUDY WITH THE UK

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A thesis submitted in fulfilment of the requirements for the award of the degree of Doctor of philosophy

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ABSTRACT

Background:

Health is a core human right. The right of health care includes access to affordable medicines. Affordability of medicines by individual patients in low-income countries is a significant factor influencing access to care and treatment. However, drug prices in low income countries are found to be higher than those in high-income countries. Although the health care system in Jordan is quite advanced in comparison to neighbouring countries, the access to affordable medicines remains problematic. It was reported that almost 80% of the public in Jordan pay for their medications through out-of-pocket payments.

High medicine prices are of a great concern to patients and their finances, which can result in poor compliance. Moreover, non-compliance can lead to reduced productivity and increased medical costs. In fact, several studies found that the high out of pocket-costs can be a significant obstacle to medical adherence with prescription medication regimens.

Aims:

The aim of this thesis is to research medicine prices and policies in Jordan, in order to recommend feasible solutions to make these affordable. To measure the affordability of medicines in Jordan and to assess the extent by which the cost of medicines is high, prices and factors affecting them were compared with the United Kingdom (UK), a high income developed country.

Methods:

A mixed-method approach was used in this thesis to research medicine prices and policies. The thesis reviewed the relevant literature, followed by reviewing the health care and pharmaceutical systems in both countries and their impact on medicine prices. Quantitative studies to measure the affordability of medicines in Jordan were conducted to assess the extent by which the cost of medicines is high in comparison to the UK and the factors that may affect medicine prices. This was followed by a qualitative study on how and why high unaffordable prices occur in Jordan. Finally, a quantitative survey exploring patients', pharmacists' and prescribing physicians' opinions towards measures that could be used to achieve greater clinical effectiveness and economic efficiency from drug prescribing was conducted. All the findings from the thesis were synthesised to form policy recommendations, designed to ensure affordable medicines for the Jordanian population.

Results and discussion:

Factors that influence prices of medicines over time were identified. These included; competition, marketing strategies, time in the market, regulations and pricing policy, change of clinical guidelines, epidemiology of disease, change in therapeutic use/value and exchange rate.

Although the income per capita is much lower in Jordan (almost 7 fold less) than the one in the UK, the studies conducted within this thesis demonstrated that medicine prices were significantly higher in Jordan compared to the UK. Generic medicines are three fold more expensive than the equivalent prices of the same drugs in the UK. However, the difference in prices for many drugs was significantly higher than the 3 fold difference. For example, the average price of pravastatin and amlodipine generics was more than eight fold higher than the UK price. Moreover, the average price of omeprazole, citalopram and fluoxetine generics were around 10 fold higher than the comparable UK price. Additionally, originator brand medicines prices were also found to be 1.5-fold more expensive in Jordan compared to the UK. Many originators were extremely higher than this average. For example, the Jordanian price of misoprostol originator tablets was around 19 times the comparable UK price. The price of ranitidine originator in Jordan was more than seven times the UK price and lansoprasole originator was around 6 times more than the price in the UK. The current pricing policy and its application are believed to be the root causes for the high prices of medicines in Jordan, as revealed by the qualitative interviews.

The expected patients' saving by using generic medicines instead of originators in Jordan ranged from 32% up to 74%. The median saving in Jordan was -30.65% compared to -71.43% in UK. The average savings were 32.68% and 43.54% in both Jordan and UK respectively. This increased to 54.96% in the UK when one outlier was removed. However, the saving calculated in both countries would have been higher if the lowest priced generic was used. An extra saving of 6.86% was identified in Jordan if the lowest priced generics were used for cardiovascular diseases (the calculated saving increased from 32.71% when using the average generic price compared to 39.57% when using the lowest priced generic).

The findings also showed a positive attitude of all stakeholders (patients, pharmacists and prescribing physicians) towards generic medications and their willingness and acceptance of strategies that encourage generic utilisation in Jordan such as generic substitution,

International Non-proprietary Name (INN) prescribing and Electronic Prescribing (EP). Such measures will help reduce the high expenditure on drugs in Jordan which accounts for around one-third of the national health care budget.

Conclusion:

A range of policy measures and changes are required to improve access to medicines in Jordan. Recommendations made included amendments to pharmaceutical policies, better enforcement of the current regulations, encouraging the use of generic medicines by introducing measures such as generic prescribing, generic substitution and public awareness education programs. These changes should result in more affordable medicines in Jordan.

Dedication

This thesis is dedicated

To

My parents

My Wife

ACKNOWLEDGEMENT

I am happy to acknowledge the inspirations of Allah, who gave me the confidence to pursue this work to its conclusion. I also would like to express my sincere gratitude to all those who gave me the possibility to complete this thesis.

I am deeply indebted to my director of study Dr. Reem Kayyali. Without her mentorship, support, and depth of knowledge, this thesis would not have been completed. Her calm, insights, compassion and elegant language were central to the conceptualisation, design, analysis and reporting of this thesis, as was her vision and ability to approach problems from a global perspective.

I would also like to acknowledge Professor Chris Cairns, my second supervisor, for his excellent comments on the research proposal, chapter 3 and chapter 4. Big thanks to my supervisor Dr. Pinnelopa Bidgood from for her guidance and invaluable suggestions in analysing the data statistically. I would like to acknowledge Mrs. Tina McKee from Kingston University for her guidance, support and the very pleasant cooperation. My thanks and appreciations also go to Mrs. Rosalind Percival for her support.

This is a great opportunity to express my respect and appreciation to my external supervisor Dr. Ibrahim Al-Abbadi from University of Jordan (Amman-Jordan), for sharing his excellent knowledge of pharmacoeconomics and pharmaceutical policy in Jordan. This person has also provided me the necessary assistance required in acquiring relevant information.

My warm thanks are due also to my friends in the UK for their encouragement and their cooperative spirit and for the nice times we spent together. Furthermore, I wish to thank all my friends, family, brothers and sisters in Jordan, without their love, support, I would never have done any of this work.

Especially, I would like to give my special thanks to my lovely wife Rinal whose patient love enabled me to complete this work. You are certainly the main contributor of all the best in my life, including this thesis. I thank God for the extraordinary chance of having you as wife, friend, companion, and even co-author. Thank you for being my best partner

and for your appreciated sacrifices. You are the reason why I always keep the spirit to finish things that I have started.

The last but not least, I would like to thank my mother whose love is boundless. I am also deeply grateful to the one whom I owe everything I am today, my father, Abdelrahim El-Dahiyat. His unwavering faith and confidence in my abilities and in me is what has shaped me to be the person I am today. I hope that this work makes you proud of me. Thank you for providing me with countless opportunities my role model. I owe my parents everything and wish I could show them just how much I love and appreciate them.

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LIST OF PUBLICATIONS ARISING FROM THIS RESEARCH

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El-Dahiyat F, Kayyali R, Abbadi I. **A COMPARISON OF GENERIC AND ORIGINATOR BRAND DRUG PRICES BETWEEN JORDAN AND THE UNITED KINGDOM**. *Jordan Journal of Pharmaceutical Sciences,* 2011 4:1

(Chapter 3 and 4)

El-Dahiyat F and Kayyali R. **EVALUATING PATIENTS' PERCEPTIONS REGARDING GENERIC MEDICINES IN JORDAN.** *Journal of Pharmaceutical Policy and Practice* 2013 6:3.

(Chapter 5)

El-Dahiyat F and Kayyali R. **COMMUNITY PHARMACISTS' PERCEPTIONS TOWARDS GENERIC MEDICINES AND THEIR OPINIONS ON FUTURE GENERIC SUBSTITUTION POLICY IMPLEMENTATION: A DESCRIPTIVE STUDY FROM JORDAN**. *Journal of Generic Medicines,* September 3, 2013 1741134313502978

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El-Dahiyat F and Kayyali R. **PHYSICIANS' PERCEPTION OF GENERIC AND ELECTRONIC PRESCRIBING: A DESCRIPTIVE STUDY FROM JORDAN**. *Journal of Pharmaceutical Policy and Practice,* 2013 (In Press)

(Chapter 5)

El-Dahiyat F, Mckee, C. Bidgood P., Kayyali R, **FACTORS AFFECTING PRICES OF DRUGS IN UK- A STUDY TYPIFIED BY MEDICINES USED FOR CARDIOVASCULAR DISEASE**. *Health Affairs,* 2013 (In Preparation)

(Chapter 3)

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El-Dahiyat F, Kayyali R, Acceptance of generic medicines in Jordan: A study of patients, pharmacists and physicians perceptions. Accepted for poster presentation - **Royal Pharmaceutical Society (RPS) Annual Conference 2013**, which will be held on Sunday 8 – Monday 9 September at the ICC Birmingham.

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GLOSSARY/ACRONYMS

(ACEIs)	Angiotensin Converting Enzyme Inhibitors
(AFR)	Annual Financial Return
(ABPI)	Association of the British Pharmaceutical Industry
(AUD)	Australian Dollar
(BNF)	British National Formulary
(CCBs)	Calcium-Channel Blockers
(CQC)	Care Quality Commission
(CDs)	Controlled Drugs
(CBA)	Cost Benefits Analysis
(CEA)	Cost Effective Analysis
(CIF)	Cost, Insurance and Freight
(CMA)	Cost Minimisation Analysis
(CQC)	Care Quality Commission
(DDD)	Daily Defined Dose
(DoH)	Department of Health
(EP)	Electronic Prescribing
(EU)	European Union
(FDA)	Food and Drug Administration
(FOB)	Free On Board
(GBP)	Great British Pound
(GDP)	Gross domestic product
(HAI)	Health Action International
(HRQOL)	Health Related Quality of Life
(int. $)	International Dollars
(IMS)	Intercontinental medicine statistics
(INN)	International Nonproprietary Name
(JUH)	Jordan University Hospital
(JNDF)	Jordan National Drug Formulary

(JD)	Jordanian Dinar
(JFDA)	Jordanian Food and Drug Administration
(KAH)	King Abdullah Hospital
(LPG)	Lowest priced generic
(MPR)	Median Price Ratio
(MoH)	Ministry of Health
(MOT)	Margin of Tolerance
(NHS)	National Health Service
(NICE)	National Institute for Health and Care Excellence
(NCE)	New chemical entity
(OTC)	Over The Counter medicines
(PMPRB)	Patented Medicines Prices Review Board
(PPRS)	Pharmaceutical Price Regulation Scheme
(PASW®)	Predictive Analytics SoftWare
(POM)	Prescription Only Medicines
(PPRS)	Price Regulation Scheme
(PPP)	Purchasing Power Parity
(QALY)	Quality Adjusted Life Years
(R&D)	Research and development
(ROC)	Return on Capital
(RMS)	Royal Medical Services
(RPSGB)	Royal Pharmaceutical Society of Great Britain
(UK)	United Kingdom
(UN)	United Nation
(UNRWA)	United Nations Relief Works Agency
(US)	United State
(US$)	United State Dollar
(VAT)	Value Added Tax
(WHO)	World Health Organisation
(WTO)	World trade organisation
(WIPO)	World Intellectual Property Organization

CHAPTER ONE

OUTLINE AND RATIONALE OF THESIS

1.1 INTRODUCTION

Health is a core human right. The right of health care includes access to essential medicines. Medicines can offer a cost effective solution to many health problems if they are of good quality, available in affordable prices and used properly.[1]

About one-third of the global population lacks reliable access to needed medicines, and this proportion can reach as high as 50% in some countries in Africa and Asia.[2] The main factor that contributes to this lack of access is the price of medicines in these countries. In developing nations, there is a lack of social insurance systems with up to 90% of people buying medicines through out of pocket payments.[3] Similar to other developing countries, access to affordable medicines, in Jordan is reportedly problematic and over 80% of the cost of medicines purchased by the public is funded through out-of pocket payments.[4]

The aim of this thesis is to research medicine prices and pricing policies in Jordan, in order to recommend feasible solutions for affordable medicine prices. To measure the affordability of medicines in Jordan and to assess the extent by which the cost of medicines is high, the prices and factors affecting them were compared with the United Kingdom (UK), a high income developed country.[5]

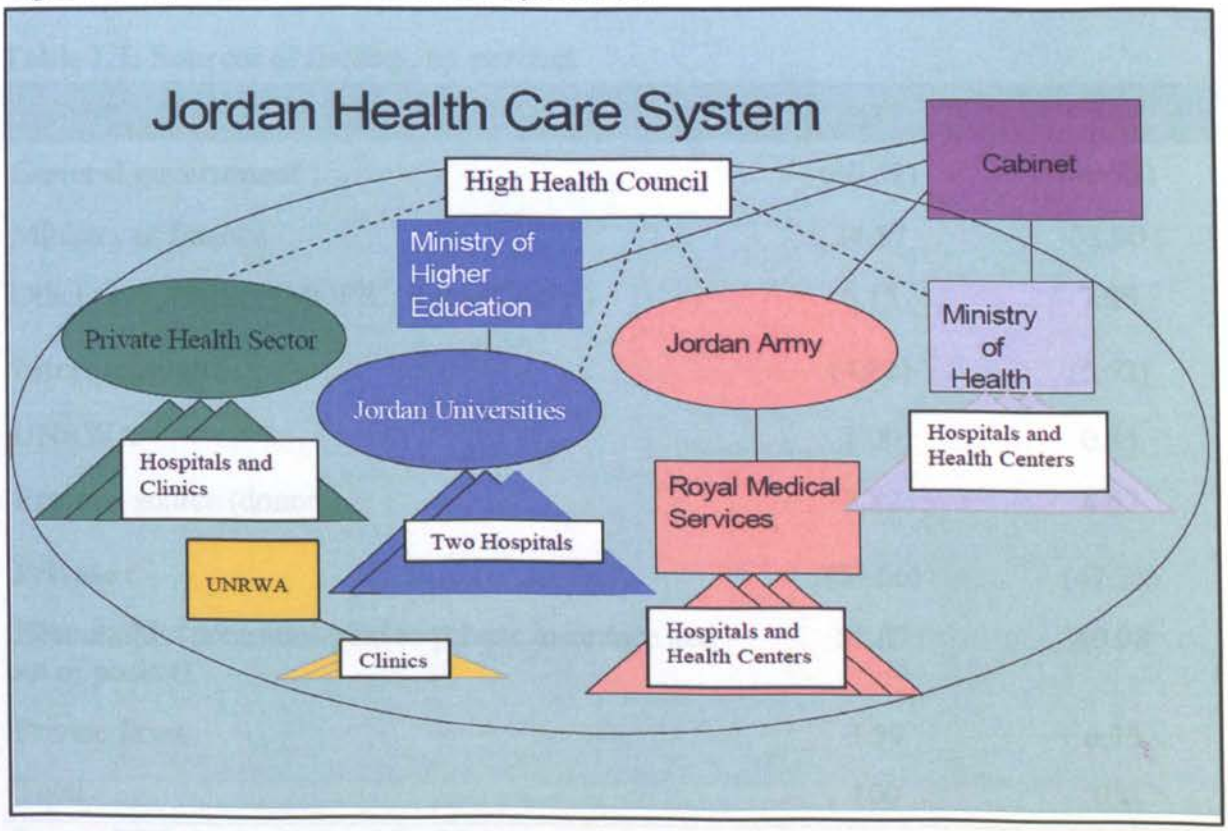
The thesis includes a review of the relevant international literature, followed by an analysis of the Jordanian health care and pharmaceutical system and its impact on medicine prices. A quantitative study of the factors that affect medicine prices in comparison to the UK, a study of medicine prices compared to the UK, followed by a qualitative study on how and why high unaffordable prices occur in Jordan will be presented. Finally, a quantitative survey study which included three questionnaires targeted at patients, pharmacists and

prescribing physicians to explore their opinions towards measures that could be used to achieve greater clinical effectiveness and economic efficiency from drug prescribing will be provided. The findings from the component parts of the thesis will be synthesised to form policy recommendations, designed to ensure affordable medicines for the Jordanian population.

1.2 BACKGROUND

Jordan has one of the most modern health care structures in the Middle East that consists of three major sectors; public, private and donors. The public sector consists of two key public programs that fund as well as delivers care; the Ministry of Health (MoH) and Royal Medical Services (RMS). It also includes other smaller public programs which contain two university based hospitals; Jordan University Hospital (JUH) in Amman and the King Abdullah Hospital (KAH) in Irbid. The widespread private sector includes 61 hospitals and many private clinics. Jordan has over 1.6 million Palestinian refugees who get access to primary care through the United Nations Relief Works Agency (UNRWA). Each of the health care sub-sectors has its own financing and delivery system (Figure 1.1).[6]

Figure 1.1: Jordan Health care sub-system [6]



The majority of the population (74%) is covered by a health service (MoH 34%, RMS 23%, UNRWA 9%, and Private Health Insurance 8%). However, the remaining 25% of population are without any form of health insurance.[6] For more detail about the Health system in Jordan, please refer to section 2.4 in Chapter 2.

1.3 HEALTH EXPENDITURE AND FINANCE

The total annual expenditure on health in Jordan was 1,381,460,034 Jordanian Dinar (JD) (United State Dollar (US$) 1,951 billion) in 2008. This represents 8.58% of the Gross domestic product (GDP) and equates to 236 JD (US$ 333) per capita.[7] The Government health expenditure in 2008 was 787 million JD (US$ 1,112 millions) which accounts for 57% of the total health expenditure and 10.16% of the total government budget, representing an expenditure of 134 JD (US$ 190) per capita. Private health expenditure covers the remaining 37.5% of the total health expenditure, while donor's health expenditure covers 5.5% of the remaining total health expenditure.[7]

The sources of finance in 2008 were 46.75% from different general governmental sources, 5.52% from international sources, such as UNRWA (0.85%) and external donors (4.67%), and 47.73% from private sources such as households (40.98%) and private firms (6.75%) (Table 1.1).

Table 1.1: Sources of finance, by percent

Source	2007	2008
General government :	(40.52)	(46.75)
Ministry of finance	34.37	38.90
Other Gov. entities (MOPIC, Royal Courts)	6.15	7.85
International:	(4.82)	(5.52)
UNRWA	1.00	0.85
External source (donors)	3.82	4.67
Private :	(54.66)	(47.73)
Households (premiums paid to private insurance and out of pocket)	51.07	40.98
Private firms	3.59	6.75
Total	100	100

Source: HHC. Jordan National Health Accounts for 2007 and 2008.[7]

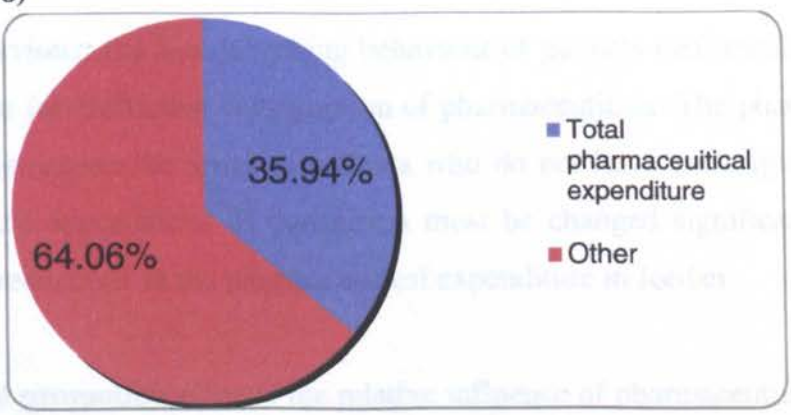
The total pharmaceutical expenditure was increased to 496,453,222 JD in 2008 from 344,899,762 JD in 2007 (Table 1.2), which represents 35.94% of the total expenditure on health (Figure 1.2) and 3.08% of the GDP (Table 1.2). This level is considered high for a middle income country.[7]

Table 1.2: Expenditures on pharmaceuticals

Expenditures type	2007	2008
Total expenditures on drugs (JD)	344.899.762	496.453.222
Per capita drug expenditure (JD)	60.3	84.86
Drug expenditures as percent of total health expenditure	34.0 %	35.94 %
Drug expenditures as percent of GDP	3.1 %	3.08 %
Distribution of drug expenditures :		
Public	11.3 %	13.81 %
Private	22.7 %	22.12 %

Source: HHC. Jordan National Health Accounts for 2007 and 2008.[7]

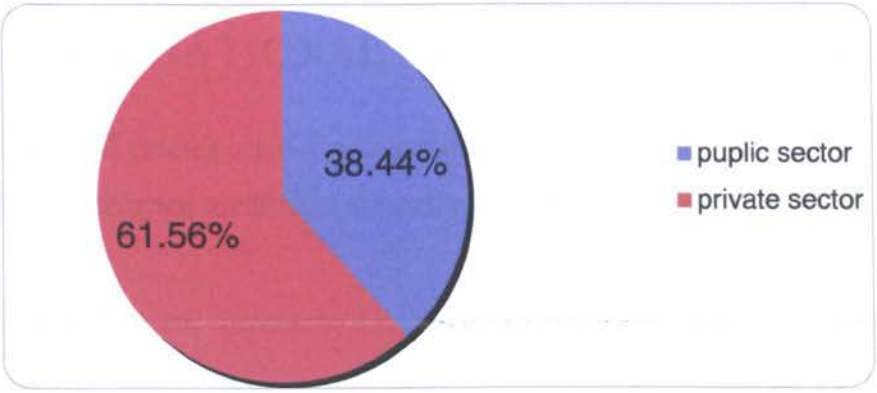
Figure 1.2: Share of total pharmaceutical expenditure as percentage of the total health expenditure (2008)



Source: HHC. Jordan National Health Accounts for 2007 and 2008.[7]

The total private expenditure on pharmaceuticals in 2008 was 305.6 million JD (US$ 431.5 million), which represents around 62% of the total pharmaceutical expenditures (Figure 1.3).[7]

Figure 1.3: Share of total pharmaceutical expenditure by sector (2008)



Source: HHC. Jordan National Health Accounts for 2007 and 2008.[7]

According to the Higher Health Council of Jordan in their national health account, the reasons included behind this high level of expenditure in the private sector are the following [7] :

Provider prescribing behaviour: the prescribing behaviour of physicians is the main factor for the high level of drug consumption in Jordan, due to the lack of sufficient pharmaceutical regulatory policies. Different medical training backgrounds for providers also lead to different prescribing behaviours.

Consumer behaviour: the health seeking behaviour of patients (self-medication practice) is a major reason for inefficient consumption of pharmaceuticals. The pharmacists tend to dispense the most expensive drugs to patients who do not have prescriptions. Therefore, the behaviour and expectations of consumers must be changed significantly in order to achieve overall reductions in the pharmaceutical expenditure in Jordan.

Pharmaceutical promotion efforts: the relative influence of pharmaceutical companies in promoting their products is extensive and uncontrolled in Jordan. Most continuous medical education within the private sector is sponsored and/or organised by the pharmaceutical industry.

1.4 WORLD HEALTH ORGANISATION (WHO)/ HEALTH ACTION INTERNATIONAL (HAI) 2004 PRICING SURVEY:

In 2004, a WHO/HAI pricing survey was conducted in Jordan to measure the availability and affordability of selected medicines according to the WHO/HAI method.[4]

The results of the survey are summarised below:

Availability

The public sector availability of originator medicines was 0%, while the availability of the lowest priced generic (LPG) medicines was 27.8%. The private sector had a higher availability of medicines (60% for originator and 80 % for generics) (Table 1.3).

Pricing

The Median Price Ratio (MPR) was used for the comparison with the international reference prices. It is expressed as a ratio of the national price to the international price.[i] Since international prices have been collected for a predefined basket of medicines, the MPR has been selected to reflect the situation in the country.

The survey found that prices in public procurement were above the international reference prices for originators; the MPR for originators was 1.38. The MPR for patients in the public sector was 5.95 for originators, while the private sector had higher prices for both originators and generics (17.05 for originators and 10.50 for generics based on LPG) (Table 1.3).

Affordability

For measuring the affordability of medicines, the number of days' of wages necessary to purchase a particular treatment for a specific condition was used. The wage considered is one paid to the lowest paid government worker in Jordan. The number of days' wages required to purchase treatment with co-trimoxazole for a child's respiratory infection was calculated to be 0.9 days' wages for the purchase of originator medicines by private

[i] The International reference price is the median of prices offered by international suppliers (both for profit and not profit) as report by MHS International Price Indicator Guide (https://erc.msh.org/mainpage.cfm?file=1.0.htm&module=DMP&language=English).For more information on the methodology WHO/HAI pricing survey, you can download a copy of the manual at https://apps.who.int/medicinedocs/documents/s14868e/s14868e.pdf

patients. However, the purchase of generic medication necessitated 10% of the day's wages for public patients and 30% of the day wage for private patients. It is evident, therefore, that generic medicines are cheaper than originator ones but are still less affordable in the private sector than in the public sector (Table 1.3).[4]

Table 1.3: Availability, pricing and affordability of medicines in Jordan

		Public procurement	Public patient	Private patient
Availability				
Median (%)	Originator		0.0	60.0
	Lowest priced generic (LPG)		27.8	80.0
Price				
Median price Ratio	Originator	1.38	5.95	17.05
	Lowest priced generic (LPG)	0.57	0.85	10.50
Affordability				
Number of days wages	Originator		-	0.9
	Lowest priced generic (LPG)		0.1	0.3

Source: WHO/HAI Pricing Survey.[4]

In this context, the present research was conducted to provide comparable, evidence-based information on medicine prices, to better inform policy makers on how to ensure affordable access to medicines for all of the Jordanian population.

1.5 AIM AND OBJECTIVES

The overall aim of this research is to recommend feasible solutions and policy recommendations to achieve more affordable medicines in Jordan. Specifically, the thesis has the following objectives:

- To assess the effectiveness of the medicine pricing policies that the Jordanian Government has put in place *via* an international pharmaceutical price comparison with the UK, a high income country (almost 7 times higher income per capita than Jordan).

- To identify the underlying factors causing high medicine prices in Jordan.

- To determine and assess the factors influencing the prices in Jordan in comparison to the UK.

- To review the current health care system in Jordan in comparison to the UK.

- To determine the Jordanian patients', pharmacists', and physicians' perceptions towards generic medicines and means that may encourage generic utilisation.

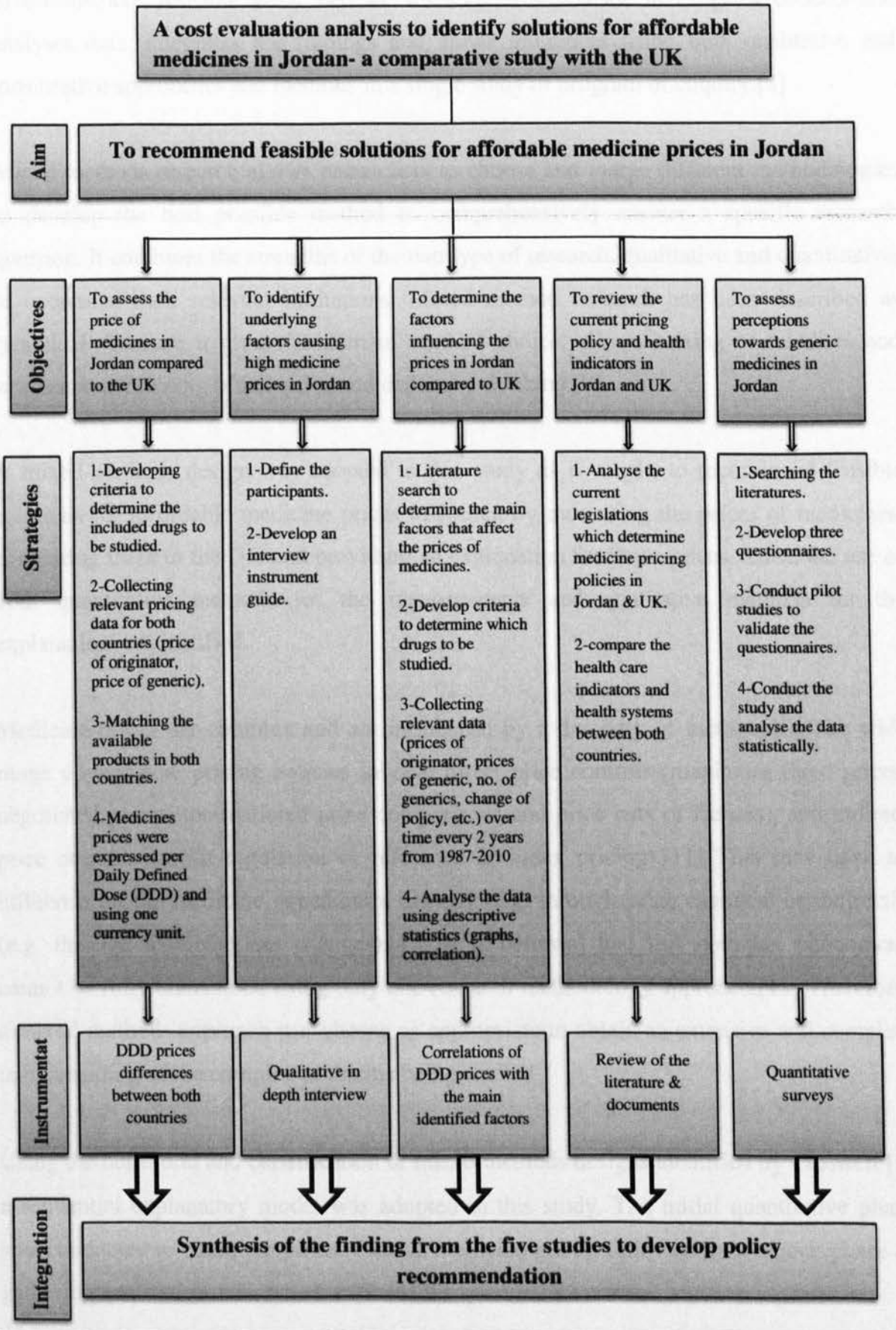
1.6 RESEARCH DESIGN AND METHODOLOGICAL CONSIDERATIONS

The main aim was divided into five different objectives to be studied using different strategies. The results from the study of the five objectives were then integrated in order to develop policy recommendations.

1.6.1 OVERALL RESEARCH DESIGN

The overall research strategy of this project is outlined in Figure 1.4.

Figure 1.4: Overall research design



1.6.2 THE RATIONALE FOR A MIXED METHODS APPROACH

Mixed-methods research is defined as 'research in which the investigator collects and analyses data, integrates the findings and draws inferences using both qualitative and quantitative approaches and methods in a single study or program of enquiry.[8]

Mixed methods research allows researchers to choose and merge different methodologies to develop the best possible method to comprehensively answer a specific research question. It combines the strengths of the two type of research, qualitative and quantitative, to overcome their relevant limitations. Mixed method research has been described as 'practical' because it gives freedom of method choice, allows mixing of numbers and words and combining of inductive and deductive thinking.[9]

A mixed-methods design was adopted in this study as it sought to recommend feasible solutions for affordable medicine prices in Jordan by measuring the prices of medicines, comparing them to the UK and providing an explanation for those prices. Thus, the use of both quantitative methods for the measurements and qualitative methods for the explanation was justified.

Medicine prices are complex and are influenced by a diversity of factors.[10] The wide range of medicine pricing policies involve direct price controls (maximum fixed prices, negotiated prices, international price comparisons and price cuts or freezes), and indirect price controls (profit regulation or reference or index pricing).[11] This may have an influence on the medicine expenditure directly (e.g. through price changes) or indirectly (e.g. through medicine use changes).[12] It is believed that this complex phenomena cannot be fully understood using only one research methodology approach.[13] Therefore, a mixed-methods approach was chosen as appropriate to obtain an extensive and complete understanding of the complex problems being studied.

Using the definition and classification of mixed methods designs identified by Creswell [9] a sequential explanatory model was adopted in this study. The initial quantitative phase was conducted to obtain empirical data on medicine prices, followed by a second phase of gathering qualitative data, which explains the quantitative results.

1.6.3 CHOOSING THE UK FOR THE COMPARISON

Normally, when making comparisons, the countries with which you compare your data should be similar in terms of economic wealth and development. However, in some cases and depending on the purpose of the comparison; comparing very poor or very rich countries can carry powerful advocacy messages, e.g. to show that the prices of medicines in a relatively poor country (Jordan in this case) are the same as a relatively rich country (UK).[14] Moreover, such a comparison can allow for recommendations to be made based on the developed country experience in rational medicine use. Furthermore, the UK is one of the reference countries used for originator brand pricing in the current Jordanian pharmaceutical pricing policy (section 2.8).[15]

1.6.4 CURRENCY USED IN THIS THESIS

To facilitate a better understanding, all money values in JD in the analysis of this study were converted to the equivalent value in the Great British Pound (GBP) using the appropriate exchange rate at that year. As a guide to relativities, the exchange rate (at January 2012) of GBP 1 is equivalent to JD 1.08 (Appendix 1).

1.7 FLOW OF RESEARCH AND INTERCONNECTION OF CHAPTERS

The thesis is organised into the following six chapters:

Chapter 1 - outline and rationale of thesis; provides the overall rationale for the thesis, introduces the research topic and objectives, background, health expenditure figures in Jordan, WHO/Health Action 2004 data on availability and affordability of medicines in Jordan and positions the overall design of the research and methodological approaches used. The chapter also outlines the thesis structure.

Chapter 2 - background of research; outlines the cost of drug development, the importance of generic equivalents, the Jordanian health system and pharmaceutical policy, the UK health system and pharmaceutical policy. It also provides a comparison, based on WHO statistical data, between Jordan and the UK. The Chapter provides an overview of the

international, academic peer-reviewed literature and the grey policy literature, along with coverage of the work of major international organisations such as the WHO.

Chapter 3 - evaluation of factors affecting the prices of medicines; presents a review of the factors affecting the prices of medicines in general and a quantitative study regarding the factors affecting prices of medicines in Jordan between 1995 and 2010 and the factors affecting prices of medicines in the UK between 1987 and 2010 in particular.

Chapter 4 - price comparisons; presents a comparison of the current prices of medicines between Jordan and the UK and a qualitative study which consists of interviews with a governmental medicine pricing authority, local industry and imported medicine wholesaler personnel representative, to explain the root cause of high medicine prices in Jordan.

Chapter 5 - use of generic medicines in Jordan: a study of patients', pharmacists' and physicians' perspective; presents the results of 3 cross sectional surveys to identify patients', pharmacists' and physicians' perceptions towards generic medicines and the introduction of a generic utilisation policy and electronic prescribing.

Chapter 6 - conclusion and recommendations; sets out the main findings from each chapter and then draws together the final conclusions and policy recommendations.

CHAPTER TWO

BACKGROUND OF RESEARCH

2.1 DRUG DEVELOPMENT

Drug discovery is an extensive, costly, complicated and high-risk development. It begins with basic research, which expands the fundamental understanding of the disease pathways and identifies and characterises new drug candidates. It is usually conducted within academic institutions, government sponsored agencies or pharmaceutical companies. Pharmaceutical medicine development is one of the crucial industries that have a huge demand on investments although the rewards may or may not come years later.[16]

New drug development takes a very long time ranging from 2 to 12 years from drug discovery until the drug is launched into the market.[17] In order to carry out drug discovery, there are a number of challenges, such as cost which is a crucial and a critical aspect in the development of drugs.[18] The cost of developing a new drug varies considerably from one drug to another and depends on the type of drug being developed. The cost will take into account any risks during development and whether the drug is based on a molecule not used before in any particular pharmaceutical product.[19]

A study by DimMasi *et al.* [20] estimated that the average cost of successfully developing a new molecular entity was US$ 802 million in 2000. This study took into account the spending on failed drug projects. The Boston Consulting Group, however, estimated the cost in 2001 as $880 million over 15 years.[21] A study published in 2006 estimated the costs of developing a new drug to vary from around US$500 million to US$2 billion depending on the therapy or the developing firm.[22] A recent study published in 2010, estimated the costs of developing a new innovative drug to reach around US$1.2 billion.[23]

Although the cost to take a new compound to market is high, its success is quite limited.[24] Only five in 10.000 compounds are believed to ever reach clinical trials and only one out of these five compounds is approved for market entry.[25]

Another crucial part of drug development is the action rates in terms of the drug development that usually exposes pharmaceutical companies to a high risk, especially when adverse news on a new compound in development can cause the share prices of the pharmaceutical companies to drop rapidly.[26] This can destroy numerous billions of dollars for shareholders instantly. In research-based drug discovery, research and development (R&D) decisions have very long-term ramifications and their impact on the market or public policy changes may not be fully realised for many years. Nevertheless, it is important to continue analysing the components and trends in the cost of pharmaceutical innovation to reach conclusions regarding its impact on both policies as well as to gain an industrial perspective.[16] In fact, one of the drawbacks/challenges of drug development that industries come face to face with is decision-making.[27] Failure of a newly developed drug during the R&D process can cause a major financial loss to the industry.[17] Pharmaceutical industries make crucial decisions, for example to terminate the R&D phase based mainly on the economy or finance. Another reason for terminating an R&D project is the lack of efficacy and safety of the drug developed that might only become evident at a later stage of the clinical phase.[27]

The pharmaceutical industry is heavily dependent on private and public investments in order to bring new products to the market. For a new drug to find its way on to the market, the establishment of basic knowledge that is related to a disease such as; the discovery of a possible treatment, the engineering of methods for drug production and the performance of tests to establish safety and efficacy are required.[17,28] The drug discovery process is summarised below [29]:

Pre-discovery

- Understand the disease

First of all, researchers from government, academia and industry contribute together to gain understanding of the disease to be treated and to identify the underlying cause of the medical problem. Recent advances in genomics, proteomics and computational power present new ways to understand illness. Although this research takes a long time and can consume many years, it can lead to frustrating dead ends. Even if the research is

successful, it will take a long period of work to turn the basic understanding of the underlying causes of disease into a new treatment.

- Target Identification

Once the researchers identify the underlying cause of a disease, they select a "target" for a potential new medicine, such as a gene or protein (single molecule), which is involved directly in a particular disease. However, it is important to choose a target that can potentially interact with, and be affected by, a drug molecule.

- Target Validation

The chosen target need to show that it is actually involved in the disease and can be acted upon by a drug. This step is crucial to help scientists avoid research paths that can lead to dead ends. This validation step is done through complicated experiments in cells and in animals.

Drug Discovery

In this stage, researchers look for a molecule, or "lead compound," that may act on their target to alter the course of the disease. This compound if successfully found after long period of time can ultimately become a new medicine.[29]

There are a different ways in order to identify such a compound [29]:

- Nature:

Researchers until now look into the natural world for interesting compounds for fighting disease. For example bacteria found in soil and mouldy plants both led to important new treatments.

- De novo:

Scientists can also create molecules from scratch by using sophisticated computer modelling to predict what type of molecule may work.

- High-throughput Screening:

This is the most common process used. Advance technologies in robotics and computational power allow researchers to test huge number of compounds against the

target. According to the results, several lead compounds are usually selected for more research.

- Biotechnology:

Engineers living systems genetically, in order to create disease-fighting biological molecules.

Early Safety Tests

A series of tests are conducted on the identified lead compounds to provide an early assessment of the safety. Tests include determining the absorption, distribution, metabolism, excretion and toxicological properties, or "pharmacokinetics," for each lead compound.

Successful drugs must be absorbed into the bloodstream, distributed to the site of action in the human body, metabolised efficiently and effectively, excreted from the body and demonstrated to be not toxic. These tests are performed in living cells, in animals and via computational models.[29]

Lead Optimisation

Having survived the initial early safety screening, the structure of lead compounds are optimised, or altered. The resulting analogues of the initial screening leads then undergo several biological and chemical tests in order to identify a final drug candidate.[29]

When a pharmaceutical company identifies a new chemical entity (NCE), patent protection needs to be acquired. According to the UK intellectual property office,[30] the definition of patent is *"An intellectual property right, granted by a country's government as a territorial right for a limited period. Patent rights make it illegal for anyone except the owner or someone with the owner's permission to make, use, import or sell the invention in the country where the patent was granted. As long as renewal fees are paid every year, a UK patent has a life of 20 years and provides protection throughout the UK, but no further."*

Once a patent has been granted, preclinical and clinical trials are initiated as follows:

Preclinical Testing

This is done before testing in human beings and consists of laboratory development, animal testing and both acute and chronic toxicity testing. Scientists carry out in vitro and in vivo tests. In vitro tests are experiments conducted in the laboratory, and in vivo studies are those in living cell cultures and animal models in order to understand how the drug works and its safety profile.[29,31]

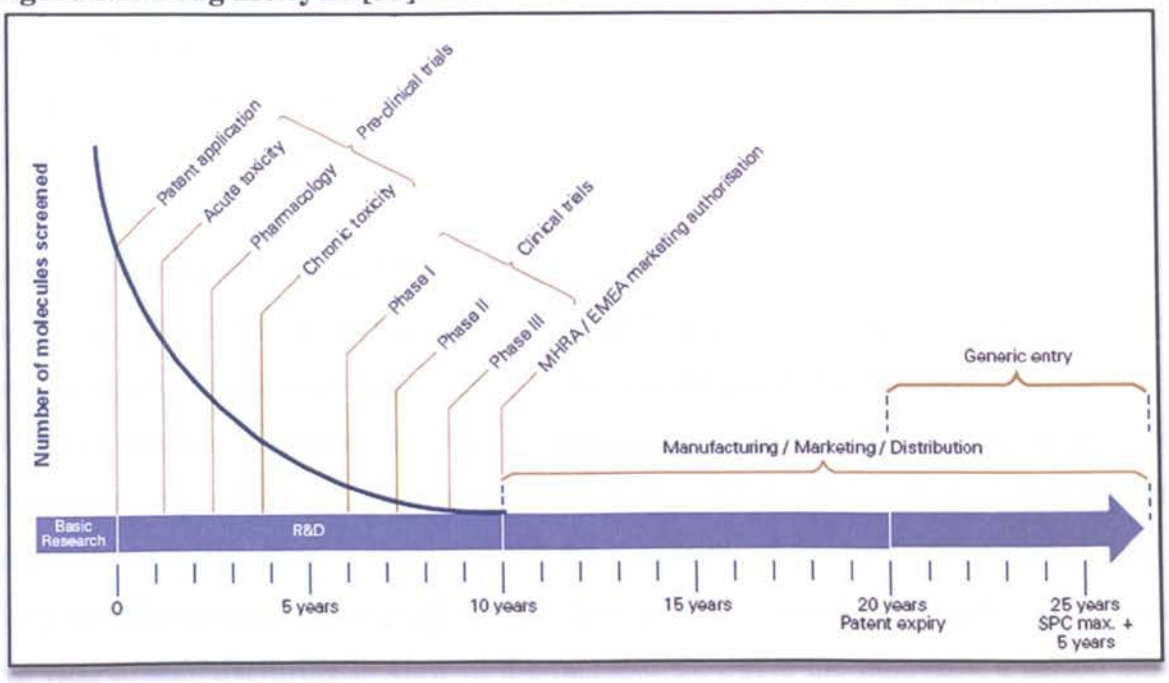
Clinical trials are carried out in humans (volunteers and patients) before drugs can receive marketing authorisation and these consist of the following stages (Figure 2.1)[31];

- Phase I trials in about 20-100 healthy adults to test the drug's safety;
- Phase II trials in about 100-300 patient volunteers to find out the safety and efficacy of the drug;
- Phase III trials on larger groups of patients (typically 1000–3000), to achieve further data on safety and efficacy.

On completion of the Phase III trials, marketing authorisation must be obtained, this usually occurs ten years after a patent has been granted (Figure 2.1).[31]

During the drug development process, it has been suggested that each clinical trial stage is considered to be more costly because of the complications of human health, compound manufacturing and treatment response.[28] Only between one to five molecules, "candidate drugs", will be studied in clinical trials out of an initial 5,000 to 10,000 compounds (Figure 2.1).[25] According to Buchanan,[19] drug development attrition rates are at their highest in the pre-clinical phase at a percentage of 60.2% and are still very high in clinical phase II at 52.1%.[27] It is believed that, at the later stages of the clinical phase of drug development, the attrition rates are at their highest; which is a big challenge for pharmaceutical companies.[27,32]

Figure 2.1: Drug life cycle.[33]



After patent expiry of the originator brand, a generic drug of the same chemical constituent which is bioequivalent to the originator brand is allowed to enter the market.[34]

2.2 WHAT IS A GENERIC MEDICINE?

As stated by Article 10-2 (b) of Directive 2001/83/EC of the European parliament [35] a generic medicinal product is; *"a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies."*.

For the purpose of this project, we will be using the definition of a generic medicine as proposed by Lewis [36] which is 'a copy of an original product whose patent has expired'. Generics on the other hand are occasionally defined as medicines 'for which the patent of the active substance has expired'.[37] Therefore encompassing all out-of-patent products including originator brands. Generics (irrespective of definition) can be marketed as branded products – with a trade name belonging to the producer – or under the generic name of the active compound.

Patents protect branded drugs from generic competition. However, they do not fully protect these drugs from other forms of originator brand competition before patent expiration, as firms can discover and patent a number of different drugs that use the same basic mechanism to cure a disease.[38]

Many studies have explained the effect of patents and other legislation on the returns to innovation, R&D and market outcomes.[39-42] In general, companies strategic decisions regarding pricing and investment aim to maximise the profit. Even though existing studies elucidate market outcomes in the pharmaceutical industry before and after patent expiration, the subject of originator brand drug survival has received relatively little attention. Actually, little is known about the capability of an originator branded drug to carry on after its entry into a market when there is competition with generic drugs. Patents are vital to manufacturing in view of the fact that they give the innovator a period during which copying can be excluded and the investment in R&D can be recovered. They are of particular importance to the pharmaceutical industry because once the chemical structure of a drug is published it is usually rather easy to copy the product. The manufacturing expenditure of a pharmaceutical is only a small part of the selling price, therefore, an imitator who has no R&D costs to recover can sell a product at a cheaper price and still make a profit.[43] Therefore, cheap medicines can be provided in form of generics, because a large portion of the cost of an originator brand drug covers the high cost of R&D. However, generic manufacturers do not have to duplicate the cost of R&D and also marketing costs conducted by originator brand manufacture, consequently, the cost of the generic drug is usually less.

2.3 THE NEED FOR GENERICS

Generics promote price competition which reduces prices in a cost effective way since generics are effective alternatives to higher priced originator pharmaceuticals. Over and above that, generics promote innovation as they remove the permanent monopoly on pharmaceutical products. This would encourage the originator companies to discover new medicines, and both originator and generic companies to develop new generic equivalents, new formulations, new dosage regimes and new methods of delivery.[44]

The essential attribute of generic drugs is that they cost less than their original brand equivalents.[45] Public and private third-party payers therefore increasingly encourage, or mandate the use of, generics through measures such as generic prescribing and generic substitution.[46]

In the UK, it was reported that more than 83% of the prescriptions in 2007 were written generically,[47] thus making the issue of generic substitution less pressing. In addition, pharmacists have an economic incentive, through supplier discounts, to dispense generic medicines.[48] In England, 68.9% of all prescription items were dispensed as generic medicines in 2011.[49]

After patent expiry, originator drug manufacturers do not necessarily compete on price at the time generic competitors enter the market, in spite of generic prices being lower than the originator price, the originator price may increase rather than decrease after patent expiry.[41,50-51] This is because that even though generics are price competitive, consumers may have loyalty to the originator brand or to another in-patent product.[51]

The continuous demand for originator branded drugs while a cheaper generic drug is available means that physicians and patients develop choice habits that are not easily changed.[52] Although, residual loyalty remains to the brand after patent expiry; it does not completely deter generic competition.[53-54] This gives rise to the term 'generics paradox' which predicts that a higher penetration by generics would not necessarily lead to a reduction in originator drug prices [55]; originator prices can increase or be maintained at their original price after generic entry.[39]

Many studies provide insights into the nature of competition in the market for pharmaceuticals after patent expiration illustrating further the 'generics paradox' phenomena. Grabowski and Vernon [41] analysed the generic entry effect in the US market on prices of 18 drugs that were first exposed to generic competition during 1983 through 1987. The statistical analysis of their data demonstrated that the branded drug price increased by an average of 7% one year following the generic entry and 11% two years after the generic entry.[41] On the other hand, generic prices dropped after first entry, the price of generic after two years of entry to the market was 35% less than the first entry price.[41] Caves [39] showed that the price of branded originator drug declines with the number of generic entrants, but the decline is small, only 4.5 %.[39]

Normally, originator drug companies increase their price when they are close to patent expiry date which makes it easier for generics to take their market share. The R&D costs can be recovered after the patent expires, if the marketing strategies are well planned. Patent expiration need not be the end of the product but with smart marketing it can be a beginning (see chapter three, section 3.1.5 for marketing strategies' details).[56]

Price regulations affecting the generic market could have an unfavourable effect on generic price reduction over time. Some studies find that countries with strict price regulation (e.g. France, Italy and Spain) have lower prices for generic drug compared to countries with a less strict regulation (e.g. Germany, Sweden and UK).[57-59] This contradicts the findings of Danzon and Chao [60] who using cross country data, suggested that regulations weaken competition in off-patent markets and that the potential cost-saving from post-patent competition is not fully realised in countries with tough price regulations.

Hudson [61] studied the relationship between patent expiration and the introduction of generics not only in the USA but also in the UK, Germany and Japan. The study showed that patent expiry does not always lead to the entry of generics, and when it does, there is usually a lag time of a few years.[62] Also, after generic entry the originator pharmaceutical company will not lose all the sales immediately, but only over a period of time. Thus, the value of a patent extends beyond the actual period of patent protection. In addition, the speed with which the original brand loses revenue would appear to be directly proportional to both the size of the market and the price of the original brand prior to generic entry.[61]

Scott-Marton [54] described the entry of generic pharmaceutical products into the market as simultaneous rather than sequential. Whereas, Bae [62] found that generic entry is slower on average in markets where there are more brand-name products competing. Furthermore, generic drug entry is faster on average in larger markets, and it is faster for drugs that mainly treat chronic diseases.

2.4 PHARMACOECONOMICS

2.4.1 INTRODUCTION & DEFINITION

The demand for and the costs of health care are increasing all over the world due to the improvement in, and sophistication of, health technologies. The escalation in health care spending is mainly because of increased life expectancy, increased technology, increased standard of living and increased demand in health care quality and services.[63] The increasing cost of healthcare products and services has become a great concern for patients, healthcare professionals, insurers, politicians and the public all over the world.[64]

The pharmaceutical costs constitute a massive part of healthcare expenditures. These expenditures have been increasing much faster compared to those of the total healthcare.[65] Health economics can be defined as the application of theories, tools and concepts of economics as a discipline to the topics of health and health care. Health economics is concerned with issues relating to the allocation of scarce resources in order to improve health. This includes both resource allocation to the health care system and to different activities and individuals within the health care system.[66]

Health care economics is intended to help decision makers make choices based on comparing expected consequences resulting from the adoption of one strategy over another.[67] Pharmacoeconomics, is the division of health care economics which describes and analyses the costs of drug therapy to the healthcare systems and society.[68] Pharmacoeconomic research is the process of identifying, measuring, comparing the costs, risks and benefits of programs, services or therapies and determining which alternative produces the best health outcome for the resource invested.[69]

Pharmacoeconomics can be defined as a tool, not a solution, which is designed to provide users and decision-makers with information about the cost-effectiveness of different pharmacotherapies. It is used in combination with the outcomes of research; a process by which different therapies or drug regimens are evaluated to measure the extent to which a goal of therapy or desirable outcome can be reached.[70] Mauskopf [71] defines Pharmacoeconomics as the *"measurement and presentation of a comprehensive set of outcomes that describe the consequences of the use of a new drug"*. Pharmacoeconomics

plays a vital role in the treatment of diseases, as it deals with both the cost and consequences of therapeutic decision making.[72] In essence, pharmacoeconomic analysis uses tools for examining the impact (desirable or undesirable) of alternative drug therapies and medical interventions.[68,73-74]

2.4.2 PHARMACOECONOMICS IN DECISION-MAKING

Pharmacoeconomic analysis has been implemented by governments and healthcare organisations to support all decision-making regarding pharmaceuticals.[75]

In order to justify various clinical decisions, including effective formulary management, the individual patient's treatment, drug use policy and resource allocation, a powerful pharmacoeconomic data tool is often used.[68,75-76]

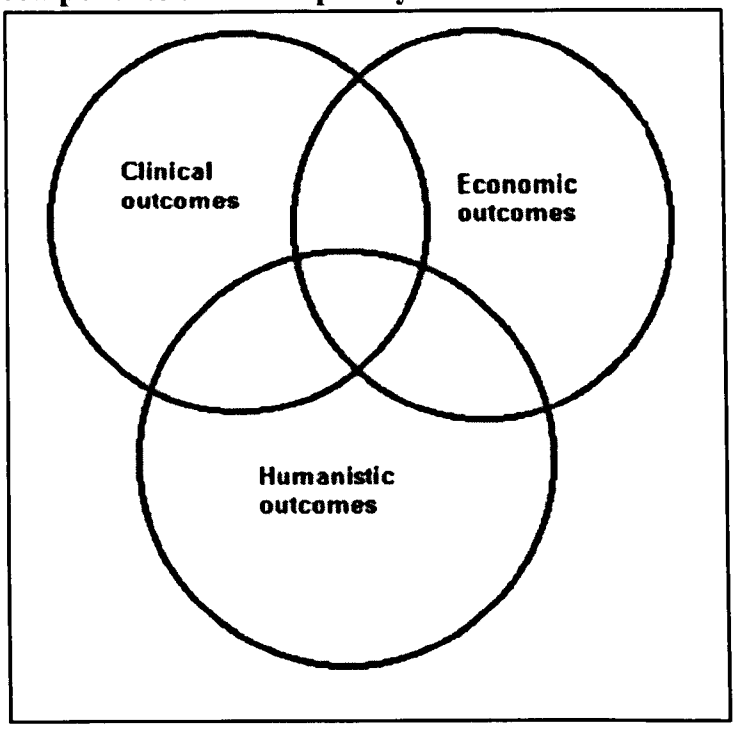
The pharmacoeconomic assessment of formulary actions is becoming a standardised practice of many pharmacy and therapeutics (P&T) committees worldwide. It can also provide the data necessary to justify that a pharmacy service maximises the resources allocated to it by hospital administrations, when competing for hospital resources. Pharmacoeconomics can provide critical cost-effectiveness data to support formulary addition or the removal of medicines. The type of medicine used and generic policy decision may have a greater impact on prescribing behaviour, if based on sound pharmacoeconomic data.

More drug companies are conducting pharmacoeconomic studies at all stages of R&D.[77-78] The use of pharmacoeconomics in the R&D process is to aid in rationalising key R&D decisions, and in guiding final pricing decisions and reimbursement planning, thereby improving resource allocations.[78] Therefore, planning for pharmacoeconomic studies should begin during the early stages of drug development as it is important that this data is available as soon as possible after a drug is launched.[77]

2.4.3 PHARMACOECONOMICS EVALUATION METHODS

Traditionally, medication decisions primarily assessed clinical outcomes (for example, safety and efficacy) of drug therapy. However, in today's healthcare environment, complete medication decisions include (if appropriate) an assessment of different types of outcomes. Figure 2.2 contains suggested components of contemporary clinical decisions.

Figure 2.2: The components of contemporary clinical decision making

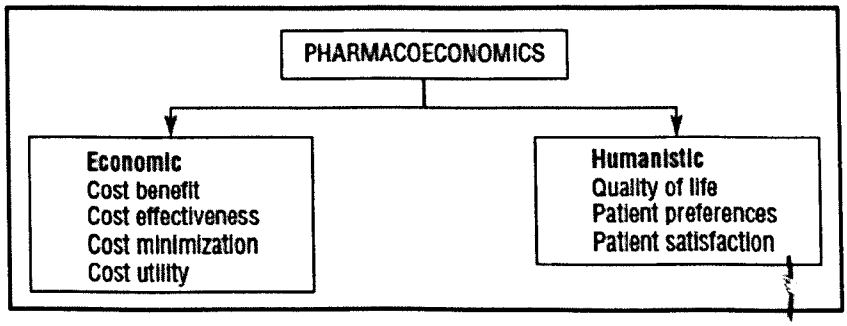


Sources: Bootman JL, Townsend RJ, McGhan WF. Principles of Pharmacoeconomics, 3rd ed. Cincinnati, OH: Harvey Whitney Books, 2005.[68]

Over the past few years some medication decisions included economic outcomes (for example, direct, indirect and intangible costs) of a pharmaceutical therapy. Most recently the humanistic cost (for example, quality of life effects) of drug therapy is included. Thus, contemporary medication decisions are multidimensional and the application of pharmacoeconomic principles and methods need to assist in incorporating such outcomes.[68]

Pharmacoeconomics constitutes both economic and humanistic outcomes evaluation (Figure 2.3).[73] Economic evaluation is however the standard method used. It is defined as 'the comparative analysis of alternative courses of action in terms of both their costs and consequences'.[69]

Figure2.3: Components of Pharmacoeconomics



Source: DiPiro, Joseph T. Pharmacotherapy: A Pathophysiologic Approach. New York: McGraw-Hill Medical, 2008. Learn more about these citation styles: APA (6th ed.)

Economic evaluation includes methods related to cost-minimisation, cost-effectiveness, cost-benefit, cost of illness, cost-utility and decision analysis, as well as quality of life and other humanistic assessments.[68,73-74].

2.4.3.1 ECONOMIC EVALUATION METHODS

There are four main types of economic health care evaluations which can be applied to pharmaceutical products (Figure 2.3). The ultimate objective of all these methods is to compare the cost and outcome of alternative regimens. The nature of outcome measurement is the important factor determining the level of complexity and sophistication as well as the reliability and validity of the comparison of alternative regimens.[67]

Pharmacoeconomics involves the utilisation of two major methodologies for health economic analysis; cost analysis and cost outcome analysis. Cost analysis considers the costs of providing healthcare products or services, but does not consider the outcomes experienced by patients or providers. Cost-outcome analysis is the most commonly used of the pharmacoeconomics methodologies as it evaluates cost in relation to outcomes. The type of analysis used depends on the nature of the problem being studied.[79]

2.4.3.1.1 COST MINIMISATION ANALYSIS (CMA)

This type of analysis evaluates cost and ignores outcome. This analysis is used only if two alternative therapies are determined to be the same with identical health benefits and therefore need not to be considered separately. The objective of this method is to select the least costly therapy among multiple equivalent interventions. It cannot be used to evaluate programmes or therapies that lead to different outcomes.[80-81] The alternatives must demonstrate equivalency in safety and efficacy (i.e. the two alternatives must be therapeutically equivalent). After confirming the equivalency in outcome, the costs can be identified, measured and compared in monetary units. CMA shows only a "cost savings" of one program or treatment over another. Examples includes comparing brands with generics, different routes of administration and different settings of administration, etc. which would achieve the same level of benefit at reduced cost.[76]

This method has been used frequently, and its application could expand given the increasing number of "me too" products (please check section 3.1.1 for the definition) and generic competition in the pharmaceutical market place.[82]

2.4.3.1.2 COST BENEFITS ANALYSIS (CBA)

A cost-benefit analysis compares the costs and outcomes of alternative treatment options in monetary terms. Cost-benefit analysis allows researchers to make comparisons across a wide variety of alternatives. It compares the costs involved in implementing a programme with the value of the outcome. Since the endpoints are measured in monetary terms, different endpoints can be studied, such as a surgical procedure compared with a pharmaceutical intervention.[68,73,81]

This analysis can be useful in strategic decision making on health care programmes. For example, nationwide immunisation programmes can be fully costed in terms of resource utilisation consumed in running the programme. This can be valued against reduced mortality and morbidity that occurred as a result of the programme.[72]

2.4.3.1.3 COST EFFECTIVE ANALYSIS (CEA)

This is the most common type of pharmacoeconomic analysis used. This analysis is used to compare two or more treatment options for a specific condition. Cost-effectiveness is dependent on the value in non-monetary terms that is placed on the outcome in relation to the cost. This analysis compares the unit of effectiveness – i.e. number of years of life saved, number of lives saved, and percentage lowering of glucose level etc. with the cost of the treatment. The results are then plotted and those treatments along the effectiveness frontier which have the lowest cost and highest effectiveness will be given preference. The treatment can be referred to as being cost effective if it has an outcome that is worth its corresponding cost in relation to alternative therapies. For example, the diuretic hydrochlorothiazide may be the most inexpensive treatment for hypertension, but it often requires a potassium supplement. The additional cost involved in the therapy means this drug is not always the most cost effective therapy.[68,79,83]

2.4.3.1.4 COST UTILITY ANALYSIS (CUA)

Pharmacoeconomists sometimes want to include a measure of patient preference or quality of life when comparing competing treatment alternatives. Cost-utility analysis (CUA) is a method of comparing treatment alternatives that integrates patient preferences and Health Related Quality of Life (HRQOL).[84] The outcome is measured in terms of changes in the patient's well-being.[85] Cost-utility analysis is performed in the same manner as cost-effectiveness analysis except that the endpoint differs. The endpoint of cost-utility analysis is described as 'quality-adjusted life years saved' (QALY). This allows cost utility analysis

to compare therapies for different diseases. Cost-utility analysis integrates both the costs and the consequences of a therapy into its comparison. Cost utility measures the final outcomes in changes of life-expectancy. This method is often used when a programme affects morbidity and mortality.[81]

CUA is the most appropriate method used to compare programs and treatment alternatives that are life extending with serious side effects (e.g. cancer chemotherapy).[86]

2.4.3.2 HUMANISTIC EVALUATION METHODS

Clinical value is the benefit of a drug which is mainly due to its clinical characteristics, efficacy and/or safety. Humanistic benefits are beneficial consequential aspects concerning or affecting the patient using the specific drug.

Pharmacoeconomic evaluations also focus on humanistic concerns. Methods for evaluating the impact of disease and treatment of disease on a patient's HRQOL, patient preferences, and patient satisfaction are all growing in popularity and application to pharmacotherapy decisions. HRQOL has been defined as the assessment of the functional effects of illness and its consequent therapy as perceived by the patient.[54] Humanistic evaluation methods assist clinicians in determining the value of pharmaceutical products, which are displayed as the physical, emotional, and social effects on the patient.[87]

In order to measure the patient's HRQOL, a patient-completed questionnaire is usually used. Many questionnaires are available, and most are either disease-specific or generic measures of health status.[88-91]

2.5 JORDANIAN HEALTH SERVICES

Among the Middle Eastern countries, Jordan is one of the countries that has the most modern health care infrastructure in the public, private and the donor sector making it a complex amalgam of three major sectors in the health care.[6]

Jordan's health care system is quite advanced although its services are mostly concentrated in the capital city Amman. Apart from Jordan having a good reputation in health services, Jordan's physicians and surgeons are proficient in English language because the Medical School is taught solely in English throughout the country. These surgeons set themselves

apart and excel through training, practicing or affiliation with top institutions in the United States, such as Johns Hopkins, the Mayo clinic and the Cleveland clinic.[92]

In 2008, more than 250,000 patients from other countries sought treatment in Jordan. The figures show that an estimated 45,000 Iraqis and approximately 25,000 patients from Palestine and Sudan, an estimated 1,500 US citizens, 1,200 UK citizens and 400 Canadians sought treatment in Jordan in that year.[93] The World Bank has ranked Jordan to be number one health care services provider in the region and among the top five in the world as well as being the top medical tourism destination in the Middle East and North Africa.[93] The recorded medical tourism related revenues exceeded one billion dollars in 2007.[93]

As explained in Chapter 1 (section 1.2), Jordan has three different health care delivery systems. The MoH which provides basic primary and secondary health services by means of a network of 29 hospitals and numerous health centres which is available for the whole population to use, the RMS which provides insurance and services through 10 hospitals to military and government personnel and their dependants, and the extensive private sector which includes 61 hospitals and many private clinics.[6,94-95] In addition to these systems, there are two large public university hospitals, which receive referrals.[96]

The public health sector, therefore, in Jordan consists of two major public programs that finance, as well as deliver care in the country namely the MoH and RMS, the other smaller public program includes several university-based programmes such as JUH.[6] Jordan has more than over 1.6 million Palestinian refugees who get access to primary care through the UNRWA.[97]

The Jordanian Government has stated that it aims to provide a comprehensive health care system, which includes the services of the private sector, to ensure preventative, tertiary and rehabilitative care for all.[98] Nevertheless, the formulation of a health care strategy and policy has been hindered in Jordan due to the disjointed nature of the health care system and lack of accurate data upon which to base development.[99]

The overall policy and strategy of the Jordanian health sector is set by the High Health Council, which is headed by the Prime Minister.[95] There are private health care insurance providers which either sell insurance policies to the individual or work with

mainly large companies to provide private insurance for their employee. According to Brosk *et al.* [99] the private sector is the largest source of health funding in Jordan which accounts for 47% of the health funding followed by the public (45%) and other donors (8%).[99]

The role of private health care is mainly confined to the urban areas and it is primarily utilised by wealthiest Jordanians.[100]

As mentioned in Chapter 1 (section 1.3), 57% of the total annual health expenditure in 2008 in Jordan were covered by the Government, with the remaining 37.5% and 5.5% being covered by the private and donor sectors respectively.[7]

On the basis of the United Nation (UN) comment number 14 on the highest attainable standard of health, Governments are to ensure the availability, accessibility, acceptability and quality of health care services.[101] Accessibility has four overlapping dimensions, non-discrimination, physical and economic accessibility, affordability and information accessibility specifically in relation to private health care providers. The UN further state that countries are obliged to ensure that privatisation of the health sector does not constitute a threat to the availability, accessibility, acceptability and quality of health care.[101]

Each of the health care sub-sectors in Jordan has its own financing and delivery system that actually reflects directly on its delivery of services among these sectors. The drawback for this system brings about problems related to accessibility, equality, duplication of services, poor coordination among major providers, un-regulation of the private sector, low utilisation rates in the private sector, limited quality improvement programs, inefficient use of available resource, poor management and an inappropriate health information system. These problems form the main challenges facing all providers of health care in Jordan.[102]

According to a WHO study conducted in 2010, 74% of the Jordanian population is covered by a health service (MoH 34%, RMS 23%, UNRWA 9%, and Private Health Insurance 8%). However, the remaining 25% of the population are without any form of health insurance.[6] Thus, while the health care system appears to function well overall, there are

still subpopulations at risk of deficient access to health care and severe financial burden, such as the poor, the elderly and the unemployed.[103]

2.5.1 REGULATION OF MEDICINES IN JORDAN

A national medicines policy has been in place since 2002 in Jordan, and the Jordan National Drug Formulary (JNDF) was published for the first time in the same year.[104] This formulary listed the essential cost-effective drugs for use within the MoH hospital facilities. The JNDF was reviewed and was republished in August 2006. In the JNDF, medicines are listed by the generic (or scientific) name.

The sale of medicines in Jordan is regulated by the Pharmacy and Drug Law as enforced by the Jordanian Food and Drug Administration (JFDA). Registration fees differ between originator brands and generics, and between imported and locally produced medicines. Generics and locally produced drugs have lower registration fees.

The public can obtain medicines from the following:

- Government pharmacies/clinics attached to health centres
- Government hospital pharmacies
- Private hospital pharmacies; these are attached to private hospitals and dispense to in-patients only
- Community pharmacies

Patients with public insurance would normally seek their medicines from a Government clinic or hospital. However, they could be referred to community pharmacies in the following circumstances [105]:

- If a patient gets a prescription from a Government clinic or hospital, and the product is on the formulary but not in stock, the clinic or hospital pharmacy stamps the prescription as considered approved but not available. The patient gets the director of the hospital to sign the prescription and then is able to go to a community pharmacy to get the product dispensed. The community pharmacy will get paid for the lowest priced brand at the JFDA rates. If a higher priced brand is dispensed, either the patient or the pharmacist will pay the difference (not likely to be the pharmacist).

- If a drug has been prescribed for the patient and it is not on the formulary, the patient must get a full medical report from the doctor. On presentation of the prescription, the pharmacist stamps it as approved and not available. The patient then goes to the insurance directorate at MoH with the doctor's report and their insurance card. The patient needs to see another MoH specialist to determine if the drug is required and if the MoH specialist approves it, the patient can go to a community pharmacy to obtain the medication.

Publicly insured patients and patients without insurance would normally approach a government institution first. Patients without insurance would be required to pay a higher co-payment than the insured public, but the cost would be significantly less than obtaining the medicines through community pharmacies. For publicly insured patients the co-payment is per product. For people covered by RMS (military personnel and their dependants), the co-payment is per prescription. The prescription covers about 5 or 6 items, which means that the payment by those covered by the RMS is significantly lower.[105]

In 2002, a circular from the Ministry of Health required doctors in Government hospitals and health clinics to prescribe generically. If prescribed by brand name, the patient gets the formulary drug anyway, unless their physician builds a case and receives special permission to have the brand name dispensed. Private health insurance companies encourage doctors to prescribe the lowest priced generic.[105]

2.6 THE HEALTH SYSTEM IN THE UK

2.6.1 INTRODUCTION

Arguably one of the most comprehensive, fair and efficient services, the National Health Service (NHS), sixty five years after its launch is now one of the largest publicly funded health services in the world.[106]

The Service is primarily funded through general taxation rather than requiring private insurance payments. The Service provide a comprehensive range of health services, the vast majority of which are free at the point of use for residents of the UK.[107] In 1948,

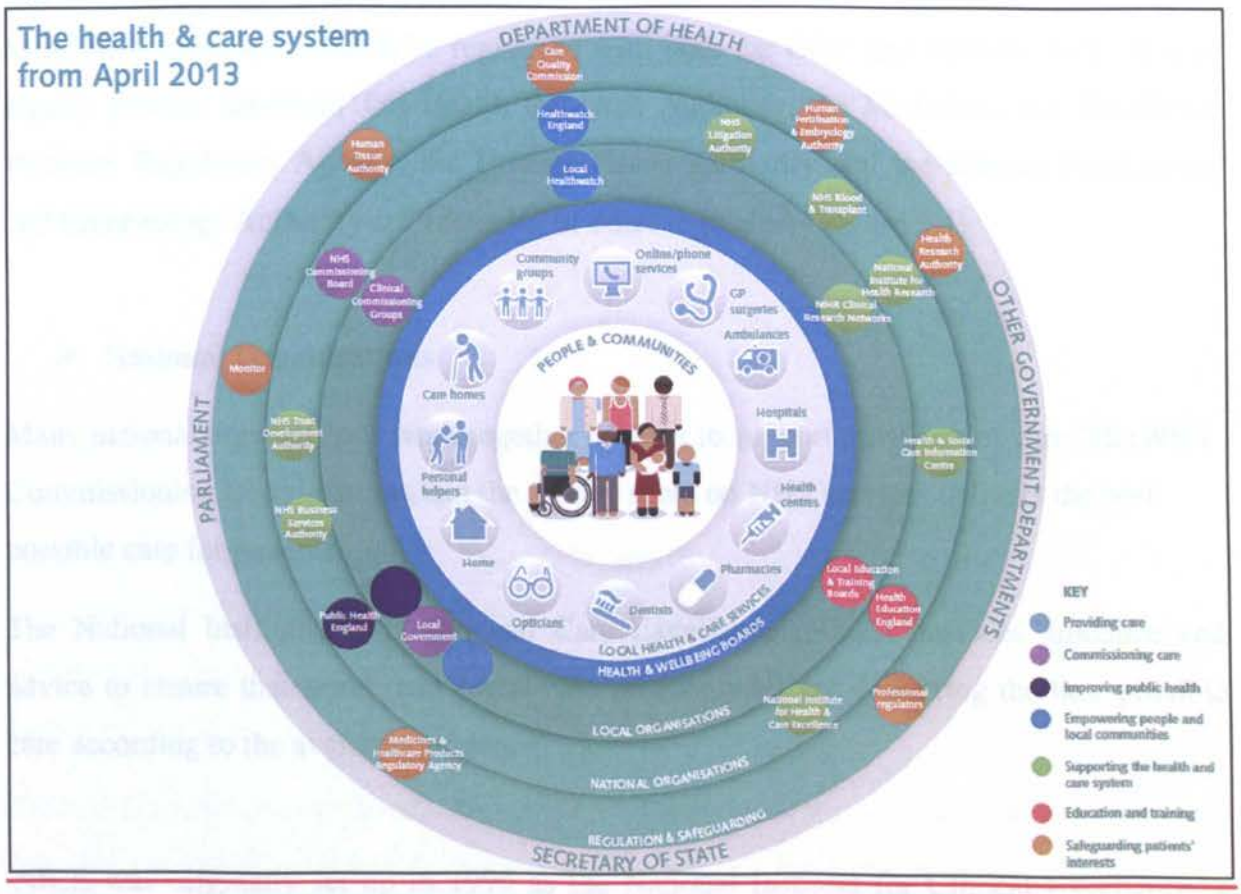
when the NHS was launched it had a budget of £437 million (roughly £9 billion at today's value). However, the budget for 2012/13 is around £108.9 billion.[106]

The NHS core principle is that good healthcare should be available to all, regardless of wealth. It covers everything from antenatal screening and routine treatments for coughs and colds to open heart surgery, accident and emergency treatment and end-of-life care.[106]

2.6.2 STRUCTURE OF NHS IN THE UK:

The structure of the NHS is shown in Figure 2.4 below, the outer layer represents the Secretary of State, Parliament, Department of Health (DoH) and other Government departments while the inner layer (heart) represents local health and care services (Figure 2.4).

Figure 2.4: The NHS structure.[106]



- **The Secretary of State, Parliament, Department of Health and other Government departments**

The main role of NHS England is to improve health outcomes for people in England. The Secretary of State for Health has the ultimate responsibility for the provision of a

comprehensive health service in England and ensuring that the whole system works together.

The strategic leadership of both the health and social care systems is the responsibility of the Department of Health (DoH) (Figure 2.4).[106]

- **Regulation and Safeguarding**

Responsibility for regulating particular aspects of health care is shared across a number of different bodies, such as the Care Quality Commission (CQC) which regulates all health and adult social care services in England, the Monitor which regulates all providers of health and adult social care services and aims to promote competition by regulating the prices and ensuring the continuity of services for NHS foundation trusts, and individual professional regulatory bodies, such as the General Medical Council, Nursing and Midwifery Council, General Dental Council and the Health and Care Professions Council. Most NHS providers need to be registered with both the CQC and Monitor to be able to legally provide services.[106] Health Research Authority, the Medicines and Healthcare Products Regulatory Agency, the Human Tissue Authority and the Human Fertilisation and Embryology Authority are examples of other regulators (Figure 2.4).

- **National Organisations**

Many national organisations work together in order to support providers of care. The NHS Commissioning Board ensures that the money spent on NHS services delivers the best possible care for patients.

The National Institute for Health and Care Excellence (NICE) provides guidance and advice to ensure that health and social care professionals are delivering the best possible care according to the available evidence.

NICE was originally set up in 1999 as the National Institute for Clinical Excellence, a special health authority, to reduce variation in the availability and quality of NHS treatments and care. After it merged with the Health Development Agency in 2005, NICE started to develop public health guidance to help prevent ill health and promote healthier lifestyles. The name was changed to the National Institute for Health and Clinical Excellence.[108]

NICE's role is to improve outcomes for people using the NHS and other public health and social care services. This is done through [108]:

- Production of evidence-based guidance and advice for health, public health and social care practitioners.

- Developing quality standards and performance metrics for those providing and commissioning health, public health and social care services;

- Providing a range of information services for commissioners, practitioners and managers across the spectrum of health and social care.

Health Education England ensures that the healthcare workforce has the right skills and training to improve the care patients receive.

Other national organisations supporting providers of care include the NHS Trust Development Authority; the National Institute for Health Research; the Health and Social Care Information Centre; NHS Blood and Transplant; the NHS Litigation Authority; and the NHS Business Services Authority (Figure 2.4).

- **Local organisations**

A range of aorganisations serve patients. Local authorities commission care and support services and also have a new responsibility to protect and improve public health and wellbeing. The budget for public health is one of the local authorities' responsibilities. Local authorities are expected to work with other health and care providers, community groups and agencies to overcome challenges such as smoking, alcohol and drug misuse and obesity (Figure 2.4).[106]

Clinical Commissioning Groups consisting of doctors, nurses and other professionals use their knowledge of local health needs in order to commission the best available services, while Local Healthwatch give patients and communities a voice in decisions that affect them.

Health and Wellbeing Boards are statutory committees of local authorities who have obligations to encourage integrated working between commissioners of services across

health, social care, public health and children's services, involving representatives of local community.[106]

- **Local Health and Care Services**

Local health and care services include hospitals, family doctors, nurses, pharmacies, dentists, opticians and online/telephone services who are the first point of contact for the public needing health care (Figure 2.4). Thus, choice is available to patients by wide range of health care providers. Health care professionals such as doctor and nurses have flexibility in the services they provide in order to meet patients' needs.

Although treatment on the NHS is free at the point of delivery, patients still encounter some costs which can be accrued for treatments for dental problems, eyesight difficulties, wig and fabric supports and prescription costs. From 1 April 2013, the charge for a single prescription item is £7.85.[109]

However, there are exceptions, for example the following groups of people can get free NHS prescriptions [106]:

- 60 years or over
- Under 16 years
- 16-18 and in full-time education
- Pregnant women, or have had a baby in the previous 12 months and have a valid exemption certificate
- Those who have a listed medical condition such as a permanent fistula, renal dialysis, cancer, diabetes, epilepsy, myxoedema, myasthenia gravis, hypoparathyroidism, hypoadrenalism and have a valid exemption certificate.
- Those who have a continuing physical disability which means they cannot go out without help from another person and have a valid exemption certificate

- Those who hold a valid war pension exemption certificate and the prescription is for their accepted disability

- An NHS inpatient

In addition, a resident or his/her partner is entitled to help if they [106]:

- Receive Income Support

- Receive Income-based Jobseeker's Allowance

- Receive Guarantee Pension Credit

- Have a valid NHS tax credit exemption certificate

- Are named on a valid HC2 (certificate for full help with health cost, [NHS low income scheme])

- Is a war pensioner, the prescription is for their accepted disablement and they have a valid war pension exemption certificate.

The following items are supplied free to every one [106]:

- Medication administered at a hospital or in a NHS Walk in Centre

- Prescribed contraceptives

- Medication personally administered by a GP

- Medication supplied at a hospital or Primary Care Trust clinic for the treatment of a sexually transmissible infection.

2.7 A COMPARISON BASED ON WHO DATA REGARDING HEALTH EXPENDITURE AND LIFE EXPECTANCY BETWEEN JORDAN AND UK

The United Kingdom is made up of England, Wales, Scotland and Northern Ireland. It is located within Western Europe. It is 243,610 square kilometres in area.[110] Its population is 62.64 million as per 2011 with a low annual population growth rate of 0.6% [5, 111]. In 2009, the average life expectancy was 79/82 years for both male and female respectively. The gross national income per capita expressed by using purchasing power parity in international dollars, PPP int. $ is 36010 as per 2011 (Table 2.1).[111]

Jordan is located within the Middle East and shares borders with numerous countries, such as Syria, Iraq, Saudi Arabia and Palestine. Jordan is relatively small in size occupying 89,342 square kilometers in area.[110] Its population is 6.181 million as per 2011 with an approximate growth of 2.6%.[5,111] The average life expectancy is 72/75 years for both males and females respectively. The gross national income per capita is PPP int. $ 5930 as per 2011 (Table 2.1).[111]

The total expenditure on health per capita was PPP int. $ 3321.67 in UK in 2011, PPP int. $ 2746.99 of which was Government expenditure. The total expenditure on health per capita in Jordan in the same year was only one sixth of UK total expenditure PPP int. $ 504.82, and the Jordanian government contribution was PPP int. $ 341.97 (Table 2.1). The WHO Figures show that the general Government expenditure on health as a percentage of total health expenditure in UK in 2011 was 82.7% which is more than the expenditure of the Jordanian Government in the same period (67.7%), the rest of health expenditure is covered by the private sector which contributes 17.3% in the UK and 32.26% in Jordan respectively (Table 2.1).[111] In terms of general government expenditure on health as a percentage of total government expenditure, this was 15.87% in the UK compared to 17.57% in Jordan (Table 2.1).[111]

The WHO data showed that the out-of-pocket expenditure as a percentage of private expenditure on health in UK was PPP int. $ 53.07 while it was PPP int. $ 76.51 in Jordan as per 2011 (Table 2.1).[111]

Table 2.1: A comparison between UK and Jordan Based on WHO data. [111]

Comparison Indicator	year	UK	Jordan
Total population (million) [5]	2011	62.74	6.181
Annual population growth rate (%)	2010	0.6	2.6
Area (sq km) [109]	2013	243610	89,342
Life expectancy at birth m/f (years)	2009	79/82	72/75
Gross national income per capita (PPP int. $)	2011	36010	5930
Per capita total expenditure on health (PPP int. $)	2011	3321.67	504.82
Per capita government expenditure on health (PPP int. $)	2011	2746.99	341.97
General government expenditure on health as a percentage of total expenditure on health	2011	82.7	67.74
General government expenditure on health as a percentage of total government expenditure	2011	15.87	17.57
Total expenditure on health as a percentage of gross domestic product	2011	9.32	8.42
Private expenditure on health as a percentage of total expenditure on health	2011	17.3	32.26
Out-of-pocket expenditure as a percentage of private expenditure on health	2011	53.07	76.51

Source: global health advisory (who) *http://www.who.int/gho/en/*

2.8 PHARMACEUTICAL PRICING POLICY IN JORDAN

The JFDA is in charge of setting the price of medicines for sale in community pharmacies (private sector). Article 11 of the Drug and Pharmacy Law [112] determines the membership of the pricing committee which includes the director of the drug directorate in the JFDA; the director of supply and purchasing; the head of the pricing department; an internist; a pharmacist specialist in pharmacology or clinical pharmacy and two experts (one being an expert in cost accounting). While the pricing committee is involved in the determination of the price of medicines distributed through community and hospital pharmacies, it is not involved in the pricing of medicines obtained through tenders.[112]

2.8.1 ORIGINATOR BRAND PRICING IN JORDAN

In Jordan, according to the pricing instructions approved by the Prime Ministry, the price of a NCE (originator brand) is allocated based on the lowest price resulting from one of the following five different methodologies [15];

- If the goods are on a Cost, Insurance and Freight (CIF) basis, the drug price to the Jordanian public is computed from the cost price on the basis of the factory-listed price in the invoice issued from the party designated to issue invoices by adding to it customs duties, bank's charges, insurance, clearing and inland transportation (plus the profits of the wholesaler, pharmacy and their administrative costs). If the basis of shipment is Free On Board (FOB), the shipping costs will be added to the above.

- The drug price to the Jordanian public is computed from the cost of the imported drug on the basis of the public price in the country of origin after deducting the Value Added Tax (VAT) there, if applicable, and after deducting the profits of wholesalers and retailers there, adding the shipping costs, bank's expenses and charges, insurance clearing and inland transportation (plus the profits of the drug store and pharmacy and their administrative costs).

- The median price resulting from the prices of the public in the following countries: UK, France, Spain, Italy, Belgium, Greece, Netherlands, Australia, Cyprus, Hungary, Ireland, New Zealand, Portugal, Czech republic, Croatia and Austria. In the event that it is not priced in all of those countries, the median price where available in not less than four countries is used.

- The price computed from the export price to the Saudi market. As for any un-registered drug in Saudi Arabia, its price in Jordan will be reviewed upon its registration there. The agent is committed to provide the JFDA with the export price to Saudi Arabia within a period not exceeding four months from the date of pricing it there.

- If the drug is registered and priced in the country of origin only and the average median public prices from the countries above becomes impracticable, then it is priced on the basis of drug prices having close chemical composition and/or therapeutic effect.

2.8.2 LOCALLY MANUFACTURED GENERIC MEDICINES PRICING

The pricing policy stated that the requested price for the locally manufactured generic medicines should not exceed 80% of the price of the originator drug when first registered and priced or upon re-pricing or 80% of its current price whichever is less.[15]

2.8.3 IMPORTED GENERIC MEDICINES PRICING

Regarding imported generic medicines, the Jordanian price is determined as the lowest price resulting from the application of the following methods [15];

- If the goods are on a CIF basis, the drug price to the Jordanian public is computed from the cost price on the basis of the factory-listed price in the invoice issued from the party designated to issue invoices by adding to its customs duties, bank's charges, insurance, clearing and inland transportation (plus the profits of the wholesaler, pharmacy and their administrative costs). If the basis of shipment is FOB, the shipping costs need to be added to the above.

- The drug price to the Jordanian public is computed from the cost of the imported drug on the basis of the public price in the Country of Origin after deducting the VAT there, if applicable, and the profits of wholesalers and retailers there and adding the shipping costs, bank's expenses and charges, insurance clearing and inland transportation (plus the profits of the drug store and pharmacy and their administrative costs).

- The export price to the Saudi market, and if it is not registered there, its pricing shall be reviewed upon its registration and the agent is committed to provide the JFDA with the price within a period not exceeding four months.

2.8.4 PRICING DECISION MAKING

The applicant has 30 days in which to appeal a pricing decision to the Director General of the JFDA. Such an appeal will be registered to the Drug Pricing Committee who has 30 days to make its recommendation. A price is considered inoperative if the applicant has not accepted it within 6 months of notification.[15]

The Director General, by a recommendation from the pricing committee, is entitled to cancel the registration of a drug or prohibit its re-registration, except after one year from its cancellation, in the event of the following breaches [15]:

- If it becomes apparent that the drug pricing was done on the basis of false information submitted by the manufacturing company or the agent.

- If the price to the public in the country of origin is reduced and such reduction was not reflected on the selling price to the Jordanian public, and the manufacturing company or its agent did not notify the committee within a period not exceeding four months from the date of the reduction.

- If the manufacturing company or its agents did not submit the export price to Saudi Arabia within four months from its pricing there, unless a document from the manufacturing company or its agent is submitted proving that the drug is not being marketed there.

The Director General of the JFDA issues a schedule of exchange rates in July each year and these are determined from the average rate for June using exchange rates published by the Central Bank of Jordan. Prices of products can be revised if the variation in the exchange rates exceeds 5% for three consecutive months.
The pricing committee revises the prices of new products after two years of registration and the price of all products are reviewed upon renewal of registration which is every five years. Where there is a price reduction in the originator drug, all generics must reduce their price, except where the price is due to an exchange rate movement or at the request of the originator country of origin's company.[15]

2.8.5 CALCULATION OF THE PUBLIC PRICE FOR DRUGS

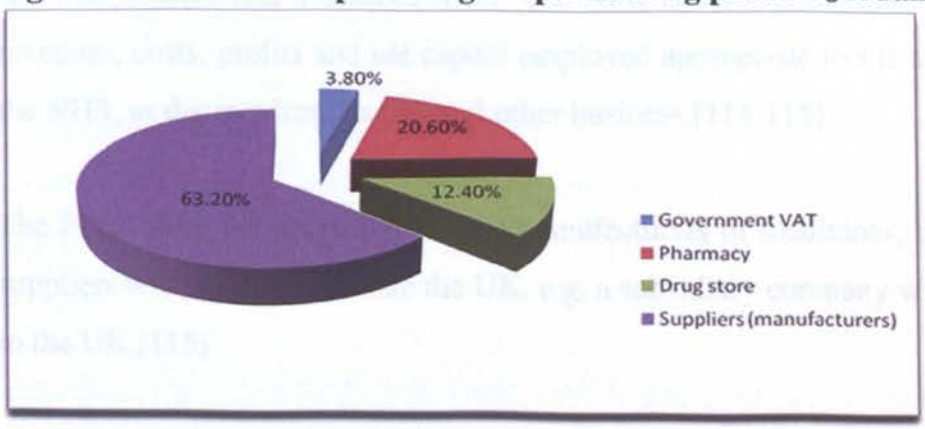
In Jordan, all pharmaceutical prices include the same margin for all products. Drug stores (wholesaler) receive 15% on the landed cost plus 4% for expenses while pharmacy receives 20% on the wholesale price plus 6% expenses. These percentages are cumulative. As a result, there are strong incentives for both wholesalers and retailers to promote and sell the highest priced drugs or brands as these attract the highest return in money terms. [15]

The public price (final selling price) of pharmaceuticals is calculated as follows (the amount of ex-factory price is illustrative):

- Ex-factory price (excluding bank charges, customs duties, insurance, clearing and inland transport and R&D costings) **£100**
- Add drug store (wholesaler) profit (15%) **£115**
- Add drug store expenses (4%) **£119.60 (cost for pharmacy)**
- Add pharmacy profit (20%) **£143.52**
- Add pharmacy expenses (6%) **£152.13**
- Add Value Added Tax (VAT) (4%) **£158.22 (public price)**

These percentages are cumulative. Thus, out of the total price of £158.22; the government receives as VAT £6.09 or 3.8% of the public price, pharmacies receive £32.53 or 20.6% of the public price, drug stores get £19.60 or 12.4% of the public price and suppliers (manufacturers) get £100 or 63.2% of the public price (Figure 2.5). Please note that as the ex-factory price excluded the bank charges, customs duties, insurance, clearing and inland transport and R&D castings, the percentage gain therefore, for each sector excluding the manufacturer will be even higher.

Figure 2.5: Cumulative percentage of public drug price in Jordan



2.8.6 BONUS PRACTICE IN THE JORDANIAN PHARMACEUTICAL MARKET

According to the JFDA website, some local manufacturers and wholesalers in Jordan provide incentives to pharmacies to stock their products.[113] These incentives are in the form of bonuses. Bonuses range between 120% and 200% and even more and are used for both the local domestic Jordanian market and the export markets. Pharmaceutical wholesalers and local manufacturer sometimes give 10 free packs of medicines for every 5 packs purchased by a pharmacy; as the pharmacy purchases more stock these bonuses increase.[113] In 2006, the JFDA tried to put a limit for this unethical practice. However, all companies opposed the proposal and the practice is still governing the Jordanian market till now.[113]

2.9 PHARMACEUTICAL PRICING POLICY IN THE UK

In the UK, the price of a new pharmaceutical product is indirectly regulated by The Pharmaceutical Price Regulation Scheme (PPRS) which is a voluntary agreement between the DoH and the pharmaceutical industry represented by the Association of the British Pharmaceutical Industry (ABPI).[114-115]

The PPRS was introduced in 1957 and is usually re-negotiated every five years. The existing scheme is for five years from January 2009. The scheme regulates the profits that companies can make from selling originator brand medicines to the NHS.
The Annual Financial Return (AFR) is the core reporting mechanism of the PPRS; the AFR is a set of audited accounts in a prescribed format, comprising primarily of a profit and loss account and a balance sheet. The AFR is used as the basis of assessment of the revenues, costs, profits and net capital employed appropriate to the supply of medicines to the NHS, as distinct from export and other business.[114-115]

The PPRS does not only apply to the manufacturers of medicines, but also applies to the suppliers with affiliates outside the UK, e.g. a subsidiary company with a place of business in the UK.[115]

The main aim of the PPRS is to set a balance to ensure that the interests of patients, the NHS, industry and the taxpayer are promoted for each other's mutual benefit. The objectives of the scheme are listed as follows [115]:

- Promote patient access and uptake for new medicines.

- Deliver value for money by securing the provision of safe and effective medicines at reasonable prices, and encouraging the efficient development and competitive supply of medicines.

- Encourage innovation as the scheme aims to promote a strong and profitable pharmaceutical industry that is both capable and willing to invest sustained R&D to encourage the future availability of new and improved medicines for the benefit of patients and industry in the UK and other countries

- Provide stability, sustainability and predictability.

Medicines are always supplied to the NHS on the basis of clinical need and cost-effectiveness where no NICE guidance exists. The Government ensures the application of NICE Technology Appraisals, and ensures that there is consistency between NICE recommendations and broader policy in the NHS. The industry and the DoH work together in order to define a set of measures that allow comparison of the uptake of all new medicines with major EU economies and provide international benchmarks and trends for the uptake of NICE approved technologies. The pharmaceutical industry recognises the need to continually improve the value for money that is achieved by the use of medicines.[115]

2.9.1 PRICING OF ORIGINATOR MEDICINES IF THE COMPANY IS A MEMBER OF THE PHARMACEUTICAL PRICE REGULATION SCHEME (PPRS) 2009

The PPRS covers all branded NHS medicines, which is defined as a human pharmaceutical product for which a marketing authorisation has been granted and to which the owner applies a brand name that enables the product to be identified without reference to its generic name.

The main elements of PPRS in order to control drug prices are explained below:

Profit control

The PPRS sets a ceiling (caps) on companies' profits on NHS sales, this means that a company can adjust the price of new drugs within its portfolio, as long as the overall profit does not exceed the cap. The Scheme sets a target cap of 21% on a company's return on capital (ROC) employed from home sales of NHS medicines.[114-115]

Research and development

The R&D cost is recognised within the prices paid for NHS medicines. The amount allowed imitates both a contribution to the worldwide cost of R&D undertaken by companies developing human medicines and a desire to reward and provide an incentive for success in R&D. This allowance is expected to contribute towards the R&D of new and improved medicines.[115]

Marketing allowance

This covers the marketing expenditure and all costs associated with the operation of marketing. Additionally, it includes the cost of all advertising, selling and promotion of a company's NHS products as well as the administrative support to such activities. Costs and activities that are expected to fall within marketing include market research and marketing strategy. However, some expenditure is not allowed as a charge in NHS prices and must be excluded from the AFR such as, samples, gifts and hospitality.[115]

Information allowance

Information expenses include all the costs of the provision and dissemination of factual information to submit to the NHS. This includes information which may or may not be required by statute, regulation or requested by a public body. Such information include non-product-specific information, support for the development, implementation or monitoring of protocols, guidelines, service standards or frameworks, and the provision to patients of support and information as required or permitted by law and the relevant code of practice. An information expense also includes the costs of samples for identification purposes, summaries of product characteristics and medical symposia.[115]

After imposing all allowances for R&D expenditure, marketing allowance, and information allowance, a maximum of 29.4% ROC can be reached.[114-115]

In the assessment of a scheme member's profit for the year, almost all cost categories are restricted. R&D, marketing and information expenses are capped at published percentage levels. Other cost categories may be restricted by negotiation. Disallowed costs are added back to profit, with the result that the assessed PPRS profit is generally higher than the profit reported by the scheme member. A scheme member whose assessed profit exceeds the target by more than 40% (the upper margin of tolerance (MOT)) is required to repay the excess or reduce prices by an equivalent amount. The upper MOT is not available in any year in which the member has been granted a price increase. Only if a member's assessed profit falls short of the target by more than 60% may the company apply for a price increase.[115]

Price Changes

The system of flexible pricing was introduced under carefully defined circumstances. Prices can change in order to reflect the value that a medicine can deliver. From 2011, small price increases were allowed. For example, if a new or additional data (i.e. new indication) is recognised, a company can request a price increase. In this case, NICE will reassess the cost effectiveness of the medicine's price.[114-115] Thus, the scheme members will seek approval of the price increase from the DoH. A minimum of eight week notice should be given. This notice should state the amount of the proposed increase and the reason in sufficient detail to satisfy the DoH that the increase is justified.[115] The DoH will not agree to a price increase unless the company's estimated and forecast profits for the current and following financial years respectively, as assessed by the Department, are below 40% of the ROC target.[115] If an increase in price is agreed, the level of the increase approved will be no more than that required for the company to achieve 65% of the ROC target for 2 year period. No company may be awarded a price increase within a period of 12 months after a preceding, authorised price increase.[115]

Price reduction on individual products may be applied differentially with some products' price being reduced by more and others by less. Audited reporting systems are in place to ensure that each member's reduction amounts to the equivalent overall price reduction across its products range.[114-115]

Monitoring and Enforcing the Scheme

The monitoring is done through the DoH in order to ensure that scheme members deliver the required price reduction over the lifetime of the scheme. In addition to the AFR

reporting set out in the independent accountants review arrangements, the PPRS provides for regular consultation between the ABPI, representing scheme members, and the DoH, representing the four UK Health Departments, as well as an arbitration process and an annual report to Parliament.[115]

2.9.1.1 PRICING OF NEW PRODUCTS

In reaching a decision on the acceptability of a price for a new product that is not introduced following the granting of new active substance marketing authorisation, the Department may take into account factors such as the following [115]:

- The price of other presentations of the same medicine or comparable products;
- Forecast sales and the effect on the NHS drugs bill;
- The clinical need for the product; and
- Any exceptional costs.

New products introduced following the granting of active substance marketing authorisation from the appropriate licensing authority may be priced on entry to the market at the discretion of the company.[115]

For any new product with a forecasted sale in any one year of the first five years following launch which are expected to exceed 20 million GBP, the company must inform the DoH of both the price and the anticipated level of sales in each of the first five years.[115]

If a company considers that the rapid uptake of a new product will cause the company to exceed the MOT, then it is obliged to inform the DoH immediately and negotiate a reduction in profitability for the current year to the upper level of the MOT. Similarly, the DoH will negotiate a reduction in profitability if it has reason to believe that the rapid uptake of a new product will cause a company to exceed the upper MOT. Thus, freedom of pricing at the time of launch of these new products is conditional on it not causing forecast profits to exceed the target profit MOT.[115]

Line extensions relating to such new products, granted on the basis of an abridged application, may also be priced at the discretion of the company provided that the application to market the line extension has been submitted to the appropriate licensing authority within five years of the grant of the original authorisation of the new product.[115]

2.9.2 PRICING OF ORIGINATOR MEDICINES IF THE COMPANY IS NOT A MEMBER OF THE PPRS

A company may choose not to become a member of the PPRS, or may be excluded if it failed to comply with scheme requirements. In these circumstances, The Health Service Branded Medicines (Control of Prices and Supply of Information) (No. 2) Regulations 2008, limit the maximum price of prescription only, branded medicines supplied to the NHS and require manufacturers and suppliers of branded pharmaceutical companies to provide the DoH with information on sales income and discounts. Members of the PPRS are exempt from such statutory powers.[115]

2.9.3 GENERIC DRUG PRICING IN UK

New generic products introduced following the granting of a marketing authorisation may be sold at a price decided at the discretion of the supplier upon entering the market, provided that the price is no more than that of the equivalent branded medicine at the date of its patent expiry.[116]

CHAPTER THREE
EVALUATION OF FACTORS AFFECTING THE PRICES OF MEDICINES

3.1 FACTORS INFLUENCING PRICES OF MEDICINES

There are many factors identified through the literature search that influence the prices of medicines.

3.1.1 THERAPEUTIC VALUE

The price of a drug is officially based on some determination of its therapeutic value and need/demands.[117] New drugs representing important therapeutic advances or therapeutically innovative drugs are priced significantly above their existing substitutes and imitative drugs are priced lower. Thus, more improved products will have higher launch prices than their established rivals, while "me-too" or imitative products will not.[118] Me-too drugs can be broadly defined as chemically related to the prototype, or other chemical compounds which have an identical mechanism of action. As soon as a prototype drug becomes available several other similarly active compounds immediately follow.[119]

Over time, drugs with highly introductory prices tend to have price reductions, whereas those with low introductory prices tend to show price increases.[120] More therapeutically advanced drugs are likely to be accepted more rapidly due to their medical and scientific importance, with less need for introductory discount to promote market penetration.[121] The evaluation of drugs' therapeutic value is conducted by NICE in the UK, whereas there is no equivalent body in Jordan.

3.1.2 R&D COSTS

The R&D costs are considered as one of the main factors which determine the price of a drug. Usually, the determined price doesn't only represent the current R&D costs to get a particular drug in the market, but it also represents a contribution to future revenues which fund future R&D investments. Product development costs are difficult to quantify as cost of failures increases R&D costs, as does regulatory delay and increasing complexity of data requirements.[122] For the entire products manufacturing cost, consideration of more than just a single product at a point in time should be made.[123] This recognises that many costs of pharmaceutical R&D and production are joint costs that cannot be allocated to individual products. Appropriateness of prices depends on return on capital, which depends on the life-cycle revenue for the full produced products.[117,123] The Companies' Law in Jordan forces companies to allocate 1% only from profit to support scientific research, which is very low.[124] Therefore, in order for industries to retain maximum profit, only generics are produced resulting in all originator brands being imported. The situation is totally different in UK, industries produce both originator and generic drugs; the PPRS confirms a commitment to recognising the cost of R&D within the prices paid for NHS disease treatments through the R&D allowance. The R&D allowance is variable, with an element providing for innovation and children's medicines.[115]

3.1.3 GOVERNMENTAL POLICIES

Some governments favour local manufacturers, by ignoring therapeutic value in setting price or simply by compensating local manufacturers more than foreign manufacturers, so that local manufacturers in these countries find it more profitable to produce drugs only for their home markets than to develop drugs for use in many countries.[117] The outcome of this industrial policy is low quality drugs (or little therapeutic innovation) from local manufacturers. Manufacturers located in countries without this industrial policy have incentives to produce high quality drugs (assuming that the market reward quality with a high price), and these high quality drugs are more likely to succeed in other markets.[117] Jordan favours local manufacturer for export markets. Many importing countries require imported products to be registered and sold using the price of country of origin as the reference price. As more than 75% of local manufacturers' production in 2007 was exported,[125] the prices of medicines in Jordan are relatively high.[4,126]

The price of medication in general is found to be significantly lower in countries that use price control regulations than countries that do not (see chapter 2 section 2.3).[127] For firms whose domestic markets use price controls, this means the price in their initial launch market is probably low, and the launch price of subsequent markets will also be lower because of parallel trade and international reference pricing.[117] Furthermore, firms headquartered in free-pricing countries that introduce a drug in a price controlled country are also less likely to launch in additional markets after that, but their initial launch is more likely to be in a country which allows for a relatively high price.[128]

A main factor that affects pricing of medicine is governmental pricing policies, some of the pricing policies and their consequences are discussed below:

- **Reference Pricing**

A number of countries use the price set for a drug in other countries as reference when setting its price. This international reference pricing means that the price in one country can affect the price in other markets. An important consequence of price controls is that pharmaceutical firms now have incentives to launch their products first in countries where they have the freedom to set a higher price, because this will influence the price in markets with price controls.[117]

Germany and the Netherlands are examples of countries in which reference pricing is used for pharmaceuticals.[129] Prices are often determined by clustering drugs by class to set a uniform rate for all drugs in the cluster. The reimbursement rates are determined through cross-country (or jurisdiction) comparisons or within country comparisons of similar therapies. The cross-country comparisons result in regulation of prices in one country which directly affect prices in another country.[129] Jordan uses reference pricing (please refer to chapter 2 section 2.8).

- **Price Ceilings**

This is a scheme whereby governments set the maximum price for the manufacturers to sell the drug. For example, The Patented Medicines Prices Review Board (PMPRB) in Canada sets the maximum price (a ceiling price) manufacturers may charge distributors, hospitals, retail pharmacy chains and others who purchase drugs in Canada directly from the manufacturer.[130] Pharmaceutical manufacturers may be fined by the PMPRB if they attempt to charge prices higher than the ceiling price.[130] The ceiling price for a generic

drug in Jordan is 80% of the registered price of its originator.[15] In the UK, the price ceiling for the new generic products is no more than that of the equivalent branded medicine at the date of its patent expiry.[116] The UK also set a ceiling on companies' profits from NHS sale (section 2.9.1).

- **Re-importation (Parallel Trade)**

Most European countries use different strategies of price controls which result in wide price variations, sometimes exacerbated by currency fluctuations.[131] These price controls have an additional effect in Europe through parallel imports, permitted between the European Union (EU). Member States since 1995, enabled wholesalers to gain price differences between EU countries by reselling pharmaceuticals to people in other nations.[131] Launching a drug in a country with strict price controls may depress global revenues if wholesalers in countries with higher prices purchase drugs in price controlled markets (with lower prices) for domestic resale. Essentially, parallel trade restricts the ability of firms to price discriminate across countries. One possible outcome is that firms serve only the higher price markets with fewer launches in low-price markets as a result of parallel trade.[117]

- **Profit Sharing**

This is a pricing by which a ceiling on companies' profits is set. This scheme is used when pharmaceutical manufacturers can accurately ascertain what portions of the profits is derived from the payer in question, for example the NHS in UK. The largest challenge in profit-sharing schemes is defining the appropriate profit limit. One example of a profit sharing scheme is the PPRS in the UK.[114-115] The PPRS regulates the pharmaceutical prices and profits of branded (non-generic) drugs in the UK for the NHS. Price and profit schemes are arrived at through negotiations every five years between the pharmaceutical industry, represented by the ABPI and the DoH. The profit-sharing scheme specifies that any profits in excess of the agreed upon ROC threshold must either be repaid to NHS, or the company must lower existing and future prices. This type of profit sharing provides a strong incentive for manufacturers to set their prices so that profits do not exceed the ROC threshold. To help enforce the ROC limits, the PPRS scheme creates a tiered system of profit reporting and financial transparency requirements (for more details please refer to chapter 2 section 2.9).

- **Value-Based Pricing**

Value-based pricing is a strategy whereby drug prices are set using a relative value metric, where each drug is compared to other drugs to assess whether the improved safety profile or efficacy is worth the additional cost.[132] Cost-effectiveness and cost-benefit analysis are both examples of relative value metrics.[132] However, although value based pricing is primarily used in conjunction with other pricing methods, in theory, this method could also operate singly and can be used by governments to establish drug prices. Traditionally, value-based pricing had a greater role in formulary development rather than a method of pricing drugs. The crux problem with this method is that the definition of "value" can be subjective. It requires establishing how much the payer will pay for improvement in health and drug safety profile and requires defining an appropriate comparison drug.[132]

Flexible pricing has been introduced in the PPRS to reflect the value which the medicine delivers. A company can request price increase once new or additional data about a medicine is recognised. NICE will then reassess the cost effectiveness of a medicine's price.[114-115]

3.1.4 PRESCRIBING AND DISPENSING HABITS

Prescribing and dispensing habits were found to have a big influence on medicine prices. According to the Jordan Pharmacy Association Law which regulates Jordanian pharmacists,[133] it is not permitted for the pharmacist to make any change or substitution to prescriptions. Doctors in Jordan usually write their prescriptions with brand name even for generics as 97% of the locally produced generics are branded generics.[134] If the pharmacist calls the doctor and requests the change, then the alternative drug can be dispensed.[135]

In the UK, it was reported that more than 83% of the prescriptions in 2007 were written generically.[47]

Some countries use demand-side controls [117] to influence prescribing and dispensing that involves either:

- A cap on the total cost of drugs a physician can prescribe (encourage doctors to prescribe a less expensive product). This is applicable to the UK.

Or

- A reference-pricing scheme [109], in which a patient is responsible for paying the price difference between his chosen drug and a reference drug.

3.1.5 COMPETITION AND MARKETING STRATEGIES

Many studies have shown that competition affects the pricing of pharmaceuticals.[34,39, 41, 51, 55,117,121,136] In fact, the current price of competitors is the first thing gathered in order for a company to set its drug price; as this information provides initial guidance for price selection. Price histories are also investigated within the same therapeutic class. Competition in pharmaceuticals exists both within drugs in particular markets (brand versus generic, within generics, prescription versus over-the counter) and between different drugs that treat the same condition regardless of patent status.[121-122] The generic segment garners significant market share within a few years of patent expiration when entry occurs.[117] The market success of a prescription medicine, other things being equal, is affected by its price relative to alternative products on the market.[121] This study should highlight the effect of competition on both brand and generic drug prices within a class and between classes in both countries.

As discussed earlier (chapter 2), after patent expiry, originator drug manufacturers do not necessarily compete on price at the time when generic competitors enter the market, in spite of generic prices being lower than the originator prices, the originator prices may increase rather than decrease after patent expiry.[41,50-51] Even if generics are priced at a competitive price, consumers may still have loyalty to the originator brand or to another in-patent product.[51] This is described as 'generics paradox' which predicts that a higher penetration by generics would not necessarily lead to a reduction in originator drug prices [55]; originator prices can increase or be maintained at their original price after generic entry.[39]

When companies set drug prices, they need to estimate the market share for their products,[137] and the factors that could influence it e.g. drug price, therapeutic advance and demand. Several marketing strategies exist. The main ones are;

- **Skimming** is the strategy of setting a high initial price and then lowering it over time; used for new products that offer significant advantages over existing ones. Sometimes, consumers overestimate the product quality. In this case, the firm will optimally "milk its reputation," which leads it to set a high launch price but then lowering its price over time.[121]

- **Penetration** is the strategy of launching a new product at a low price and then raising it over time; for products that represent only marginal improvements over their established counterparts.[121,138] The critical factor when marketing new product is the buyers' lack of knowledge about it. This leads the seller to set low introductory prices to encourage use and build up reputation.[138]

The skimming strategy is more likely to apply in "acute" circumstances while penetration in "chronic" conditions.[121]

- **Parity:** the product is viewed as little or no different from current competitors and is priced equivalent to the prevailing level.[121,138]

3.1.6 ECONOMIC FACTORS:

Exchange rates or PPPs are the relevant basis for currency conversion. Exchange rates determine the innovator firm's actual net revenues from foreign sales in terms of domestic currency, and hence the relative country's contributions to financing R&D. Moreover, if foreign prices are converted at PPPs, opportunities for parallel trade occur whenever exchange rates fall relative to PPPs.[139] In Jordan, according to the pricing policy of medicines, the exchange rates are revised in July each year and if the variation in the exchange rates exceeds 5% for three consecutive months the price of drugs get revised.[15]

Compliance with the daily dose all the length of therapy is a growing concern and a source of unrealised revenue. [140] In theory, the ability of the patient to afford the drug (drug affordability) must be taken into account when setting the price; as patients who are unable to afford a medication will often not take it. Therefore the income per capita should be taken into consideration when setting drug prices in a country.

3.1.7 TYPE OF DISEASE AND ITS PREVALENCE

In theory, prices of drugs for a certain condition should be reflective of the prevalence of that disease in that country. For example the price of Hepatitis B medications should be cheaper in Jordan than in UK, because of the prevalence of Hepatitis B which is much more prevalent in Jordan than the UK.[141] Furthermore, patients are willing to pay for drugs which treat symptomatic or acute conditions for example, arthritis or infections, however patients complain from the cost of a medicine for an asymptomatic such as

hypertension.[142] As a result, retail pharmacy in the US usually apply lower margin of profit for medications that treat chronic conditions than those for acute conditions.[143]

3.1.8 PRICE DISCRIMINATION

Price discrimination is "a policy where a seller sets different incremental margins on various units of the same or similar products."[144] In most markets, price differentiation is a tool that allows manufacturers to incorporate the differences in the willingness to pay or the ability to pay for their product or service by different customer segments into their pricing strategy.[145]

Regarding pharmaceutical products, differential pricing (also called tiered pricing) is the adjustment of product prices according to the purchasing power of patients in different geographical or socioeconomic segments. It is a very effective strategy to improve access to essential medicines in low and middle income countries. In such countries high proportions of patients purchase their medicines using out of pocket payments and therefore cannot afford prices compared to high income markets.[146]

According to a study conducted by Lichtenberg [147] patients in the lowest income bracket usually pay 25% less for pharmaceuticals compared with patients in high income bracket. On the other hand, patients in the middle income bracket pay 6% more than high income patients.[147] This could be explained by the different degrees of price discrimination that manufacturers use.

Pharmaceutical companies also use "third degree price discrimination," which in this case means giving discounts for volume depending on variations in disease burdens among countries.[148]

3.2 CURRENT STUDY

This study was adopted from a previous study conducted by the same researcher,[126] in which the effects of competition and time in the market for 5 drugs were studied (omeprazole, lansoprazole, simvastatin, enalapril and lisinopril). El-Dahiyat *et al.* [126] found that the price of the originator drugs investigated decreased when the first generic for the same drug or the same class of drug was introduced in the UK. On the other hand,

originator drug prices did not change when the first generic was introduced in Jordan. However, there was no apparent correlation between number of generics available or number of years of availability of generics on the market and the prices of the drugs investigated in Jordan and in the UK. This stimulated an investigation into factors and trends influencing pricing of medications used for long term conditions. As the main aim of this chapter is to study the effect of competition on drug pricing, therefore the effect of the number of originators and number of generics on the mean price of each was studied. Moreover, in order to fully evaluate the effect of competition, the change of trends with the length of availability in the market was investigated, the length on the market may reflect different marketing strategies. The availability or lack of trends will be explained in light of other factors influencing pricing.

3.3 METHODS

3.3.1 DRUG SAMPLE SELECTION

Drugs in this study were selected according to the following inclusion and exclusion criteria:

Inclusion criteria:

- Drug used for chronic medical condition.

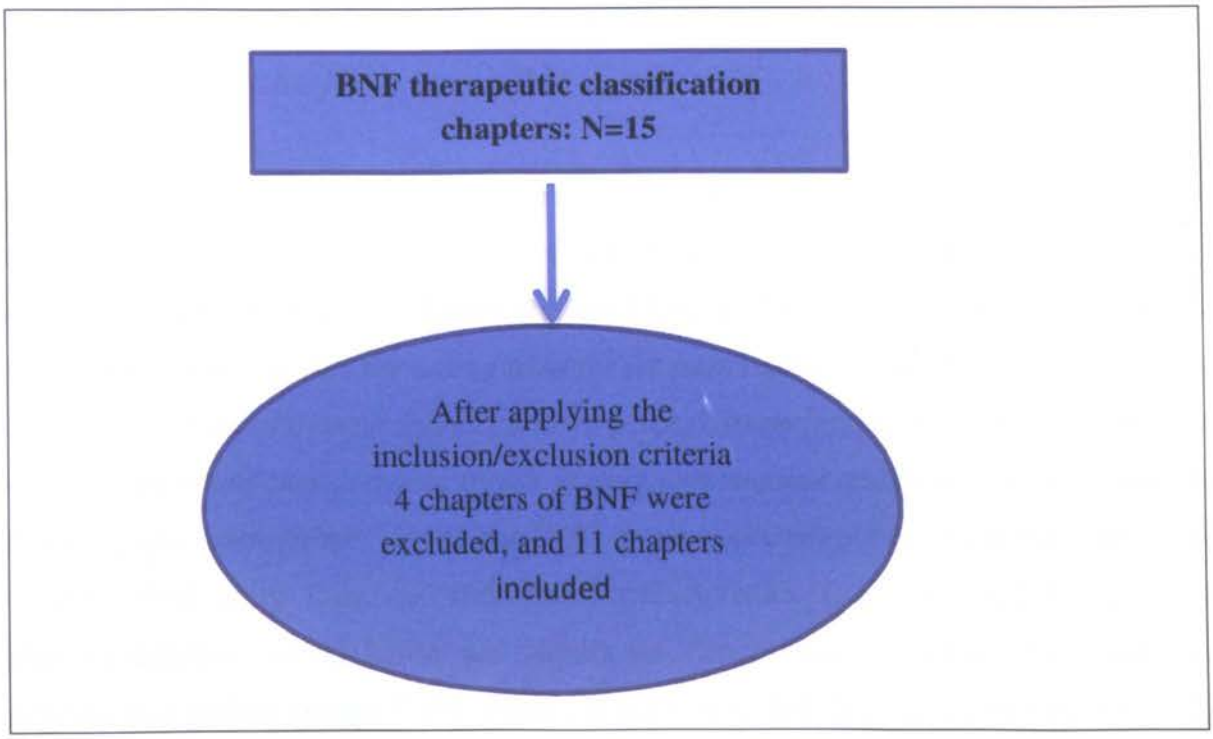
Exclusions criteria:

- If a drug is already available as a generic in 1987, as the effect of generic launch on originator price cannot be determined from the BNF.
- Controlled drugs (CDs).
- Modified or sustained release preparations.
- Drugs which are less suitable for prescribing based on UK guidelines in March 2010.
- Parenteral drugs.

- Combination products.
- Drugs for which brand specific prescribing is required based on UK practice e.g. diltiazem and insulin.
- Drugs for acute conditions and drugs for treatment of acute exacerbation of chronic conditions e.g. oral steroids and nebules.
- If an originator was withdrawn before a generic appeared e.g. etodolac (a non-steroidal anti-inflammatory drug (NSAID) used for rheumatic disease).
- Drugs that are not prescribed and dispensed in the community e.g. Human immunodeficiency virus (HIV) drugs.
- If an originator brand couldn't be identified e.g. isosorbide mononitrate.
- Medical devices e.g. peak flow meters.
- Drugs available as British Pharmacopeia formula e.g. aqueous cream.
- Drugs not used for a chronic medical condition e.g. oral contraceptive and drugs for substance dependence.
- Agents used as food for enteral nutrition or foods for special diets.

The following chapters of the BNF were completely excluded; infections, immunological products and vaccines and anesthesia, as the products listed within them are not mainly used for chronic conditions (Figure 3.1).

Figure 3.1: Flow diagram of the BNF therapeutic chapters' selection process



After applying the inclusion/exclusion criteria on the included 11 chapters of the BNF, 307 active ingredients from 81 different therapeutic classes were included to be studied (For more details about included and excluded classes and drugs, please refer to Appendix 2). The matching active ingredients in Jordan were 187, from 64 different therapeutic classes.

3.3.2 COLLECTING AND HANDLING DATA

For each of the 307 medications, the retail price of the originator and the average retail price of generics available were collected over time.

The prices of originators and generics for the included active ingredients in the UK were collected every 2 years (13 time points) using the BNF editions from 1987 until 2010. The BNFs used were accessed from the library archive of the Royal Pharmaceutical Society of Great Britain (RPSGB).

Jordanian drug prices were collected every 2 years from 1995-2010 (9 time points) due to the unavailability of previous data. The prices were collected from two different sources. The prices for the years 2010, 2009 and 2007 were collected from the JFDA pricing directorate. However, the prices from 1995-2005 were collected using the Intercontinental Medicine Statistics (IMS) health reports for Jordan.

The Chemist and Druggist generic lists were used to collect the number of generics in the UK and it was accessed from the library archive of RPSGB. Jordanian numbers of generics were collected from the JFDA and the IMS reports.

As the drugs pack sizes vary between the two countries, all collected prices were converted and expressed as daily defined doses (DDDs). According to the WHO Collaborating Centre for Drug Statistics Methodology, the DDD is defined as *"the assumed average maintenance dose per day for a drug used for its main indication in adults, DDDs provide a fixed unit of measurement independent of price, currencies, package size and strength enabling the researcher to assess trends in drug consumption and to perform comparisons between population groups"*.[149] The DDD does not necessarily reflect the recommended or prescribed daily dose, as individual characteristics (e.g. age and weight) and pharmacokinetics consideration are significant determinants of doses for individual patients and patient groups.[149] DDD for each included drug was obtained from the WHO Collaborating Centre for Drug Statistics.[149] Certain preparations do not have established DDDs. These include topical products, sera, vaccines, antineoplastic agents, allergen extracts, general and local anaesthetics and contrast media. Therefore, for ophthalmic preparation (i.e. eye drops), the DDD was assumed to be 5ml and for topical preparations (i.e. ointments/creams) the DDD was assumed to be 1 gram.

The prices per DDD were calculated by choosing the same strength of the DDD or the easiest way to achieve the DDD. For example, if a drug is available in two different strengths, 5 mg and 10 mg and the DDD is 15mg, the strength that is easier to match the DDD which is 3 tablets of 5mg rather than 1.5 tablets of 10mg was chosen.

As the BNF lists the mean price for all generics available, a similar strategy was adopted in Jordan. The mean DDD prices of originators and generics were calculated, together with the total number of originators and generics available for each therapeutic class at each time point. The Jordanian prices were expressed in JD per DDD and UK prices were expressed as GBP per DDD.

3.3.3 DATA ANALYSIS

The collected accumulated prices from all BNF chapters included in the whole data set were tested for normal distribution. The whole data set was not normally distributed according to both graphical presentation and the results of Kolmogorov-Smirnov test of

normality. However, for each therapeutic class (sub-cluster) the data was close to normal distribution. Therefore, it was decided to study the drugs according to their therapeutic classes. 81 and 64 therapeutic classes were studied in UK and Jordan respectively.

Data was analysed using Predictive Analytics Software (PASW 18®). Pearson correlations were used to study the correlation between prices of both originators and generics with the number of originators, number of generics and the length of time in the market for each class singly. Previous research adopted a similar statistical method.[150] A P value of <0.05 was considered statistically significant.

Other factors were also analysed by studying the trends of prices over time in light of disease epidemiology, competition within a class and between classes, marketing strategies, change of therapeutic value, etc. To illustrate these factors, the cardiovascular system was studied as it represents around 30% of the included drugs and classes in both countries. Figures illustrating the prices of originator and generic if available vs. time for each drug in both countries were plotted using Microsoft Excel program. By studying these graphs (drug by drug), new factors that might influence the pricing of medicines were identified.

3.4 RESULTS AND DISCUSSION

3.4.1 PEARSON CORRELATION BETWEEN NUMBER OF ORIGINATORS AND PRICES

Table 3.1 shows Pearson correlation between the number of originators and the prices of originators and generics in both countries.

The majority of therapeutic classes, 21 out of 64 and 31 out of 81 in Jordan and UK, respectively, showed positive relationships between the mean price of originators in the class and the total number of originators in the same class. The classes that showed significant positive correlations in both countries are anticoagulant, corticosteroids inhalers, antimuscarinic bronchodilators, dopaminergic drugs used in parkinsonism and other anti-diabetic drugs classes (Table 3.1).

In general, therapeutically innovative drugs are priced higher than existing substitute while imitative drugs are priced lower.[118] Newly released innovative originators usually

launch at higher prices which leads to increase of the average prices of the current ones, this is due to the fact that new drugs representing important therapeutic advance are priced significantly above their existing substitutes.[118]

Other therapeutic classes showed negative correlation between the mean prices of originators in the class and the total number of originators in the same class in both countries such as proton pump inhibitors and statins ($p<0.05$). In Jordan, angiotensin converting enzyme inhibitors (ACEIs) and NSAIDs showed negative correlations. Angiotensin receptor antagonists, calcium channel blockers (CCBs) and selective serotonin inhibitors showed negative correlations in the UK (Table 3.1). The common feature of these drugs is that they are "me-too" drugs. This group of drugs have lower launch prices than their established rivals as they do not provide any therapeutic advancement.[118] "Me too" drugs use introductory discounts to promote market penetration in order to be accepted more rapidly. [118]

Only few classes, 8 in both countries, showed negative correlation between the number of originators and mean price of generics. On the other hand, 8 and 12 classes showed positive correlation in Jordan and in the UK respectively (Table 3.1). Only 2-3 classes showed significant correlation between the number of originators and the price of generic as shown in table 3.1. Moreover, there was no class that had the same significant correlation in both countries.

In summary, more classes showed a positive correlation between the mean price of originators and the number of originators in both countries. In Jordan 21 from 64 of the studied classes showed positive correlations, from which 17 were statistically significant. Similarly, 26 classes in the UK showed significant positive correlations out of 81 classes. The findings highlight, although not conclusively, that new, innovative or therapeutically advanced medicines e.g. inhalers or new anti-coagulant or new anti-diabetic, are still priced high and not affected by other originators within a class due to their therapeutic advancement and need to recoup the high R&D costs. However, "me too" drugs' prices are affected by their available competitors in the market leading to a reduction in their prices to ensure market penetration and share. It appears that there is little influence from the number of originators on price of generics. This could be due to generic pricing being regulated to be cheaper than originator price in most countries,[151] hence being less sensitive to number of originators but rather price of originators. However, the findings

indirectly show the benefits of generic existence as they remove the permanent monopoly on pharmaceutical products by enhancing innovation and drug discovery which is reflected in the high number of originators within a class.[44]

Table 3.1: Correlations between number of originators in the class and prices of medicines

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Gastro-intestinal system								
H-2 Receptor antagonist	a	a		0.035	a	a	a	a
Chelates & complexes	0.926**		a	a	a	a	a	a
Prostaglandin analogues	a	a	a	a	a	a	a	a
Proton pump inhibitors		0.908**		0.901**		0.705*	a	a
Aminosalicylate	a	a	0.967**		a	a	0.258	
Affecting immune			a	a			a	a
Cardiovascular system								
Thiazide diuretic	a	a	a	a	a	a	a	a
Loop diuretic	a	a	0.985**		a	a	a	a
Potassium sparing diuretic	a	a		0.352	a	a	0.132	
Anti-arrhythmic drugs		0.964**	0.824**		a	a	a	a
Beta-adrenoceptor blocker drugs	0.557		0.907**			0.182	0.348	
Vasodilator antihypertensive drugs			0.966**				0.726**	
Centrally acting antihypertensive drugs	a	a	a	a	a	a	a	a
Alpha-adrenoceptor blocking drugs		0.936**	0.760**			0.813	a	a
Angiotensin-converting enzyme inhibitors		0.856**		0.016		0.705*		0.350
Angiotensin-II receptor antagonists	0.770*			0.864**		0.623	a	a
Renin inhibitors	a	a	a	a	a	a	a	a
Calcium-channel blockers	0.644			0.631*	0.545		a	a
Other antianginal drugs	a	a	0.941**		a	a	a	a
Peripheral vasodilators	a	a	0.516		a	a		0.243
Anticoagulant and protamine	1.000**		0.997**		a	a	a	a
Antiplatlet drugs	a	a	0.974**		a	a		0.686*
Antifibrinolytic drugs	a	a	a	a	a	a	a	a
Statin		0.875**		0.978**		0.325	a	a
Ezetmibe			a	a			a	a

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Bile acide sequestrants	a	a	0.071		a	a		0.675
Fibrates	0.08			0.075	0.521		a	a
Nicotinic acid group			a	a			a	a
Respiratory system								
Adrenoceptor agonists		0.985**	0.983**		a	a	a	a
Antimuscarinic bronchodilators	0.827*		0.986**		a	a	a	a
Corticosteroids	0.985**		0.833**		a	a	0.074	
Cromoglicate & related therapy	a	a	a	a	a	a	a	a
Leukotriene receptor antagonist	a	a	0.963**		a	a	a	a
Central nervous system								
Antipsychotic drugs	0.928**		a	a	0.823		a	a
Antipsychotic 2nd generation drugs				0.962**			a	a
Antimanic drugs	a	a	a	a	a	a	a	a
Tricyclic and related antidepressant	1.000**			0.821**	a	a		0.457
Monoamine-oxidase inhibitors			a	a			a	a
Selective serotonin reuptake inhibitors				0.739**				0.110
Other antidepressant drugs	0.999**		0.385		0.750		1.000**	
CNS stimulants and drugs used for attention defects hyper activity disorder	a	a	0.907**		a	a	a	a
Drug used for obesity		1.000**		0.082	a	a	a	a
Prophylaxis of migraine	a	a	a	a	a	a	a	a
Control of epilepsies	0.523		0.690**		0.865**		0.368	
Dopaminergic drugs	0.997**		0.911**		a	a	0.765**	
Antimuscarinic drugs used in parkinsonisms	a	a		0.667*	a	a	a	a
Drugs used in essential tremor , chorea, tics, and related disorders	a	a	0.917**		a	a	a	a
Drugs for dementia	0.871*			0.915**	a	a	a	a
Endocrine system								
Sulphonylureas	a	a		0.147	a	a		0.422
Other antidiabetic drugs	0.974**		0.936**		a	a	a	a
Treatment of hypoglycaemia			a	a			a	a
Antithyroid drugs	a	a	a	a	a	a	a	a
Calcitonin and parathyroid hormones	a	a	a	a	a	a	a	a
Bisphosphonates & other drugs		0.035		0.930**		0.799	a	a
Bromocriptine & other drugs	a	a	0.990**		a	a	0.340	

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Obstetrics, gynaecology and urinary-tract disorders								
Drugs for urinary retention		1.000**	0.963**		0.995**		a	a
Drugs for urinary frequency	0.995**		0.937**		a	a		0.781*
Malignant disease and immunosuppression								
Antiproliferative immune-suppressants	a	a	a	a	a	a	a	a
Other immunomodulating			a	a			a	a
Progestogens	1.000**		a	a	a	a	a	a
Hormone antagonists		1.000**		-0.434	a	a	a	a
Gonadorelin analogues	0.995**		0.864**		0.500		0.621	
Nutrition and blood								
Iron overload	a	a	a	a				
Sickle cell disease			a	a				
Carnitine deficiency			a	a				
Nephropathic cystamine			a	a			a	a
Tyrosinaemia type_1			a	a			a	a
Urea cycle disorders				0.993**			a	a
Homocystinuria			a	a			a	a
Other metabolic disorder			a	a			a	a
Musculoskeletal and joint diseases								
Non-steroidal anti-inflammatory drugs		0.887**	0.424		0.578		0.388	
Drug that suppress the rheumatic process	a	a	0.990**		a	a	a	a
Long term control of gout			a	a			a	a
Enhance neuromuscular	a	a	a	a	a	a	a	a
Skeletal muscle relaxant	a	a	0.900**		a	a	0.113	
Eye								
Beta blocker	0.842**			0.333		0.880**	a	a
Prostaglandin analogues		0.751		0.968**	a	a	a	a
Carbonic anhydrase inhibitor	0.968**		0.920**		a	a	a	a
Sympathomimetic	a	a	0.838**		a	a	a	a
Skin								
Preparation for psoriasis		0.963**	0.43		a	a	a	a
Drug affecting immune response	0.995**		a	a	a	a	a	a
Total								
Classes with correlation	21	13	31	20	8	8	12	8
Classes with significant correlation	17	11	26	12	2	3	3	2

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

a Cannot be computed because at least one of the variables is constant.

3.4.2 PEARSON CORRELATION BETWEEN NUMBER OF GENERICS AND PRICES

From the statistical analysis shown in table 3.2, the correlations between number of generics and the mean price of originators were mainly negative especially in "me too" classes; 15 and 19 classes showed such correlation in Jordan and UK with 9 and 10 of them being statistically significant, respectively. Many classes showed this trend in both countries such as; proton pumps inhibitors, statins, H2 receptor antagonists and ACEIs (Table 3.2). This trend suggests that competition between originators and generics exists within drugs in the same class and between different chemicals that treat the same condition. This has been documented in various papers.[121-122]

The negative correlation between number of generics and originator prices in Jordan was similar to a recent study published in 2013, which found that the absolute price of originator brand medicines in South Africa declined as the number of generic equivalents in the market increased.[152] Furthermore, a study by Caves [39] showed a small decline in originator price with the increase of the number of generics entrants. A study by Bergman and Rudholm [153] based on Swedish data, analysed the impact of competition between brand-names and generics using data on 18 substances for the period (1972-1996), they find that the price of the brand-name is lowered by competition.[153] Studies also found that the number of branded substitutes appears to have a negative effect on launch prices of new products.[121,154]

Interestingly, 24 classes in the UK compared to 7 in Jordan showed positive correlation between number of generics and originator price, however only 9 and 2 of these were statistically significant in the UK and in Jordan respectively. This trend supports the concept of "generic paradox" whereby the increase in number of generics does not necessarily translate into a drop of the price of originator but rather an increase.[55] Other studies showed that originators price increase rather than decrease after patent expiry.[41, 50-51] Some originator drug companies increase their price close to patent expiry to allow generics to take their share in the market.[56] Furthermore, most originator companies have marketing strategies that allows them to recoup R&D costs and make enough profit prior to patent expiry, hence don't have any stimulus to reduce their prices after generic entry. However, they rely on customer loyalty; private patients in different markets and their other products range to keep making enough profit to sustain the production of that originator product. Hence, their originators are less sensitive to generic competition.

With regards to the correlation between number of generics and price of generics, one cannot conclude a clear trend as similar number of classes showed positive and negative correlation in both countries (Table 3.2).

Table 3.2: Correlations between number of generics in the class and prices of medicines

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	Positive	negative
Gastro-intestinal system								
H-2 Receptor antagonist		0.853**		0.736**		0.603		0.514
Chelates & complexes		1.000**	a	a		1.000**	a	a
Prostaglandin analogues	a	a	a	a	a	a	a	a
Proton pump inhibitors		0.748*		0.887**		0.593		0.710
Aminosalicylate	a	a	0.449		a	a	0.238	
Affecting immune			a	a			a	a
Cardiovascular system								
Thiazide diuretic	a	a	0.575*		a	a		0.394
Loop diuretic	a	a	0.671*		a	a	0.630	
Potassium sparing diuretic	a	a	0.518		a	a		0.582*
Anti-arrhythmic drugs	a	a		0.444	a	a	0.471	
Beta-adrenoceptorblocker drugs		0.503	0.615*		0.824**		0.519	
Vasodilator antihypertensive drugs				0.127				0.357
Centrally acting antihypertensive drugs	a	a		0.632	a	a	0.983*	
Alpha-adrenoceptor blocking drugs		1.000**	0.397			0.813	0.449	
Angiotensin-converting enzyme inhibitors		0.859**		0.686**		0.482		0.045
Angiotensin-II receptor antagonists	0.544		a	a		0.228	a	a
Renin inhibitors	a	a	a	a	a	a	a	a
Calcium-channel blockers		0.44		0.737**	0.264			0.788
Other antianginal drugs	a	a	a	a	a	a	a	a
Peripheral vasodilators	a	a	0.417		a	a		0.322
Anticoagulant and protamine	a	a	a	a	a	a	a	a
Antiplatlet drugs	0.114			0.206	0.688			0.336
Antifibrinolytic drugs	a	a		0.940**	a	a	0.687	
Statin		0.767*		0.846**		0.690	0.788	
Ezetmibe			a	a			a	a
Bile acide sequestrants	a	a		0.195	a	a	0.223	
Fibrates		0.435	0.734**		0.178			0.461
Nicotinic acid group			a	a			a	a

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	Positive	negative
Respiratory system								
Adrenoceptor agonists	a	a	0.402		a	a	a	a
Antimuscarinic bronchodilators	a	a	a	a	a	a	a	a
Corticosteroids	a	a	0.417		a	a	0.492	
Cromoglicate & related therapy	a	a	0.447		a	a		0.500
Leukotriene receptor antagonist		0.886	a	a		1.000**	a	a
Central nervous system								
Antipsychotic drugs	0.745		0.693**		0.288		0.379	
Antipsychotic 2nd generation drugs				0.49				0.867
Antimanic drugs	a	a	a	a	a	a	a	a
Tricyclic and related antidepressant	a	a	0.866**		a	a	0.594	
Monoamine-oxidase inhibitors				0.583			0.787	
Selective serotonin reuptake inhibitors				0.842**				0.690
Other antidepressant drugs	0.780*		0.21		1.000**		a	a
CNS stimulants and drugs used for attention defects hyper activity disorder	a	a	a	a	a	a	a	a
Drug used for obesity	a	a	a	a		1.000**	a	a
Prophylaxis of migraine	a	a		0.900**	a	a		0.781*
Control of epilepsies		0.404	0.501		0.935**		0.539	
Dopaminergic drugs	a	a	0.840**		a	a	0.686*	
Antimuscarinic drugs used in parkinosinosim	a	a		0.202	a	a		0.142
Drugs used in essential tremor , chorea, tics, and related disorders	a	a	a	a	a	a	a	a
Drugs for dementia	a	a	a	a	a	a	a	a
Endocrine system								
Sulphonylureas		0.525		0.467		0.937**		0.800*
Other antidiabetic drugs		1.000**	a	a		1.000**	a	a
Treatment of hypoglycaemia			a	a			a	a
Antithyroid drugs	a	a	0.304		a	a	a	a
Calcitonin and parathyroid hormones	a	a	a	a	a	a	a	a
Bisphosphonates & other drugs	0.14			0.842**		0.928**		0.988
Bromocriptine & other drugs	a	a	0.083		a	a	0.094	

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	Positive	negative
Obstetrics, gynaecology and urinary-tract disorders								
Drugs for urinary retention		0.972**	0.518		0.954**		0.961**	
Drugs for urinary frequency	a	a	0.707**		a	a	0.671	
Malignant disease and immunosuppression								
Antiproliferative immune-suppressants	a	a	a	a	a	a	a	a
Other immunomodulating			a	a			a	a
Progestogens	a	a	a	a	a	a	a	a
Hormone antagonists	a	a	a	a	a	a	a	a
Gonadorelin analogues	0.498		0.304		1.000**			0.803*
Nutrition and blood								
Iron overload	a	a	a	a				
Sickle cell disease			a	a				
Carnitine deficiency			a	a				
Nephropathic cystamine			a	a			a	a
Tyrosinaemia type_1			a	a			a	a
Urea cycle disorders			a	a			a	a
Homocystinuria			a	a			a	a
Other metabolic disorder			a	a			a	a
Musculoskeletal and joint diseases								
Non-steroidal anti-inflammatory drugs		0.825*	0.034		0.816**			0.069
Drug that suppress the rheumatic process	a	a	a	a	a	a	a	a
Long term control of gout			0.605*				0.773*	
Enhance neuromuscular	a	a	a	a	a	a	a	a
Long term control of gout								
Skeletal muscle relaxant	a	a	0.331		a	a	0.233	
Eye								
Beta blocker	0.885**			0.762**		0.973**		0.409
Prostaglandin analogues	a	a	a	a	a	a	a	a
Carbonic anhydrase inhibitor	a	a	a	a	a	a	a	a
Sympathomimetic	a	a	a	a	a	a	a	a
Skin								
Preparation for psoriasis	a	a	a	a	a	a	a	a
Drug affecting immune response	a	a	a	a	a	a	a	a
Total								
Classes with correlation	7	15	24	19	10	13	20	20
Classes with significant correlation	2	9	9	10	6	7	4	4

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

a Cannot be computed because at least one of the variables is constant.

3.4.3 PEARSON CORRELATION BETWEEN THE TIME (YEARS) AND PRICES

Table 3.3 illustrates Pearson correlation between the effect of time in the market and the prices of originators and generics in both countries.

The correlations between the effect of time in the market and the mean prices of originators of 29 and 28 drug classes mostly the "me too" classes in Jordan and UK respectively showed a decrease in price as the time in market increased (e.g. statins, H_2 receptor antagonists and proton pump inhibitors). As discussed earlier, imitative "me-too" drugs usually have lower launch prices than their predecessors as they do not provide any therapeutic advancement.[118] Moreover, "me too" drugs use introductory price discounts to promote market penetration so as to be accepted more rapidly.[118] As the number of years in the market increase, the number of originator and generics within a class also increase, thus the decrease in price observed can be due to competition. Furthermore, most pricing policies review prices of drugs periodically based on predefined criteria. Such strategies can also lead to price reduction over time. The price reduction observed also could also be due to a skimming marketing strategy, which introduces the drug at a higher price and then decrease it over time.[121]

Other classes (21 and 44 in Jordan and UK respectively) showed positive relation between mean price of originators and time in years. Over time, the average price of available originators increased. Interestingly, almost the same classes showed positive correlation between time and price of originator in Jordan, also showed positive correlation between the numbers of originators and price (19 out of 21). This is an expected trend as the newly innovative drugs are usually therapeutically improved and priced at higher prices than the ones already in the market. The price of a drug is officially based on some determination of therapeutic value and need/demands.[117-118] New drugs representing important therapeutic advance are priced significantly above their existing substitutes.[118] Moreover, the cost of drugs will continue to increase over the years as they become more selective and more difficult to be produced. The cost of newer drugs reflects the R&D spending [19] (chapter 2, section 2.1). The increase in price could also be due to a penetration marketing strategy, where a low introductory price secure share in the market but the price is then increased when customer confidence and loyalty is established.[121,138]

Regarding the correlation between the effect of the years and the prices of generics, more classes in both countries showed negative correlation rather than positive one, 14 and 26 in Jordan and UK with 8 and 11 of them being statistically significant respectively (Table 3.3). Such a negative correlation was shown by a study conducted by Grabowski and Vernon [41] which showed that generic prices for 18 drugs investigated after 2 years of entry into the market was 35% less than their first entry price.

Table 3.3: Correlations between the time in years and prices of medicines

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Gastro-intestinal system								
H-2 Receptor antagonist		0.959**		0.848**		0.807**		0.758**
Chelates & complexes	0.737*			0.823**		1.000**	a	a
Prostaglandin analogues		0.457		0.889**	a	a	a	a
Proton pump inhibitors		0.813**		0.975**		0.631		0.795
Aminosalicylate		0.630	0.812**		a	a	0.476	
Affecting immune			0.811**				a	a
Cardiovascular system								
Thiazide diuretic		0.682*	0.743**		a	a		0.581
Loop diuretic		0.346	0.703**		a	a	0.777*	
Potassium sparing diuretic	a	a	0.934**		a	a		0.079
Anti-arrhythmic drugs		0.834**		0.594*	a	a	0.234	
Beta-adrenoceptorblocker drugs		0.799**	0.786**		0.914**		0.472	
Vasodilator antihypertensive drugs			0.928**				0.803**	
Centrally acting antihypertensive drugs		0.635		0.864**	a	a		0.924
Alpha-adrenoceptor blocking drugs		0.709*	0.461			0.280		0.059
Angiotensin-converting enzyme inhibitors		0.855**		0.515		0.552		0.288
Angiotensin-II receptor antagonists	0.765*			0.985**		0.524	a	a
Renin inhibitors	1.000**		a	a	a	a	a	a
Calcium-channel blockers		0.758*		0.777**		0.013		0.866*
Other antianginal drugs	a	a	0.610		a	a	a	a
Peripheral vasodilators	a	a	0.619*		a	a		0.497

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Anticoagulant and protamine	1.000**		0.669*		a	a	a	a
Antiplatlet drugs	0.333		0.831**		0.705			0.732**
Antifibrinolytic drugs	a	a		0.621*	a	a		0.968*
Statin		0.831**		0.949**		0.756*	0.924*	
Ezetmibe			a	a			a	a
Bile acide sequestrants		0.155	0.126		a	a		0.531
Fibrates		0.523	0.566*		0.001			0.308
Nicotinic acid group			0.771**				a	a
Respiratory system								
Adrenoceptor agonists		0.923**	0.873**		a	a		0.945
Antimuscarinic bronchodilators	0.717*		0.945**		a	a	a	a
Corticosteroids	0.815**		0.654*		a	a	0.397	
Cromoglicate & related therapy	a	a	0.447		a	a		0.500
Leukotriene receptor antagonist		0.795	0.753			0.945	a	a
Central nervous system								
Antipsychotic drugs	0.858**		0.979**		0.251		0.744**	
Antipsychotic 2nd generation drugs				0.929**				0.988*
Antimanic drugs	a	a		0.891*	a	a	a	a
Tricyclic and related antidepressant	0.875**		0.954**		a	a	0.552	
Monoamine-oxidase inhibitors				0.877**				0.980**
Selective serotonin reuptake inhibitors				0.918**				0.782
Other antidepressant drugs	0.944**		0.379		0.869*			1.000**
CNS stimulants and drugs used for attention defects hyper activity disorder	a	a	0.861**		a	a	a	a
Drug used for obesity		0.679		0.706		1.000**	a	a
Prophylaxis of migraine	a	a		0.869**	a	a		0.778*
Control of epilepsies	0.449		0.743**		0.856**		0.308	
Dopaminergic drugs	0.905**		0.894**		a	a	0.799**	
Antimuscarinic drugs used in parkinosinosim	a	a		0.177	a	a	0.753**	
Drugs used in essential tremor , chorea, tics, and related disorders	a	a	0.842**		a	a	a	a
Drugs for dementia	0.757			0.818*	a	a	a	a

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Endocrine system								
Sulphonylureas		0.553		0.349		0.937**		0.926**
Other antidiabetic drugs	0.897**		0.845**			1.000**	a	a
Treatment of hypoglycaemia			0.718**				a	a
Antithyroid drugs		0.650	0.827**		a	a	a	a
Calcitonin and parathyroid hormones		0.869	a	a	a	a	a	a
Bisphosphonates & other drugs	0.162			0.968**		0.919**		0.945
Bromocriptine & other drugs		1.000**	0.820**		a	a	0.753**	
Obstetrics, gynaecology and urinary-tract disorders								
Drugs for urinary retention		0.865**	0.745**		0.770*		0.883**	
Drugs for urinary frequency	0.934**		0.948**		a	a		0.689
Malignant disease and immunosuppression								
Antiproliferative immune-suppressants	a	a		0.933**	a	a	a	a
Other immunomodulating			a	a			a	a
Progestogens	0.875**		0.709**		a	a	a	a
Hormone antagonists		0.809*		0.826*	a	a	a	a
Gonadorelin analogues	0.784*		0.518		0.558			0.931**
Nutrition and blood								
Iron overload	a	a	a	a				
Sickle cell disease			a	a				
Carnitine deficiency			a	a				
Nephropathic cystamine			0.774*				a	a
Tyrosinaemia type_1			a	0.756			a	a
Urea cycle disorders			a	0.627			a	a
Homocystinuria			a	a			a	a
Other metabolic disorder			a	0.920			a	a
Musculoskeletal and joint diseases								
Non-steroidal anti-inflammatory drugs		0.790*	0.253		0.838**			0.263
Drug that suppress the rheumatic process	a	a	0.914**		a	a	a	a
Long term control of gout			0.777**				0.579	
Enhance neuromuscular	a	a	0.938**		a	a	a	a
Skeletal muscle relaxant		0.707*	0.672*		a	a	0.161	

Therapeutic class in each body system	price of originator				price of generic			
	JORDAN		UK		JORDAN		UK	
	correlation coefficient				correlation coefficient			
	positive	negative	positive	negative	positive	negative	positive	negative
Eye								
Beta blocker	0.901**			0.906**		0.940**		0.939**
Prostaglandin analogues		0.630		0.925**	a	a	a	a
Carbonic anhydrase inhibitor	0.785*		0.802**		a	a	a	a
Sympathomimetic		0.774*	0.594*		a	a	a	a
Skin								
Preparation for psoriasis		0.849**	0.232		a	a	a	a
Drug affecting immune response	0.677		a	a	a	a	a	a
Total								
Classes with correlation	21	29	44	28	9	14	16	26
Classes with significant correlation	16	17	35	21	5	8	8	11

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

a. Cannot be computed because at least one of the variables is constant.

3.4.4 PEARSON CORRELATION BETWEEN THE PRICES OF ORIGINATORS AND THE PRICES OF GENERICS

Table 3.4 shows Pearson correlation between the prices of originators and the prices of generics in both countries.

In general, more classes showed a positive correlation between the mean price of originators and the mean price of generics in both countries. In Jordan, 15 of the studied classes showed positive correlations, of which 6 were statistically significant (Table 3.4). Similarly, 27 classes in the UK showed significant positive correlations, of which 10 were statistically significant (Table 3.4).

The positive correlation was expected in Jordan as the generic pricing policy in Jordan links the generic price with the originator price, as it states that the requested generic price should not exceed 80% of the originator price.[15] The positive correlation observed in the UK was also expected partly due to the pricing policy which state that generic prices cannot exceed branded medicines' prices at time of their patent expiry.[116] Moreover, the healthy competition environment between originators and generics in the UK market could have resulted in price of generics being parallel to those of originators.[155,60]

There was a negative correlation shown between prices of generics and originators for 7 and 14 classes of medicines in Jordan and UK respectively, with the price of originator increasing as the price of generic decreased. This could be explained by marketing

strategies and the "generic paradox" concept discussed previously.[55,121] A study found that originator price increased, whereas those of generics decreased two years after generic entry which mimic the negative correlation observed.[41]

Table 3.4: Correlations between the price of originator and the prices of generics in both countries

Therapeutic class in each body system	JORDAN		UK	
	correlation coefficient			
	positive	negative	positive	negative
Gastro-intestinal system				
H_2- Receptor antagonist	0.869**		0.819**	
Chelates & complexes	1.000**		a	a
Prostaglandin analogues	a	a	a	a
Proton pump inhibitors	0.673*		0.596	
Aminosalicylate	a	a	0.087	
Affecting immune			a	a
Cardiovascular system				
Thiazide diuretic	a	a		0.370
Loop diuretic	a	a		0.790*
Potassium sparing diuretic	a	a		0.065
Anti-arrhythmic drugs	a	a		0.018
Beta-adrenoceptorblocker drugs		0.633	0.398	
Vasodilator antihypertensive drugs			0.795**	
Centrally acting antihypertensive drugs	a	a	a	a
Alpha-adrenoceptor blocking drugs	0.813		0.569	
Angiotensin-converting enzyme inhibitors	0.794*		0.269	
Angiotensin-II receptor antagonists		0.160	a	a
Renin inhibitors	a	a	a	a
Calcium-channel blockers	0.417		0.966**	
Other antianginal drugs	a	a	a	a
Peripheral vasodilators	a	a	0.699	
Anticoagulant and protamine	a	a	a	a
Antiplatlet drugs	0.717			0.529
Antifibrinolytic drugs	a	a	0.879	
Statin	0.608			0.269
Ezetmibe			a	a
Bile acide sequestrants	a	a		0.608
Fibrates	0.578			0.086
Nicotinic acid group			a	a
Respiratory system				
Adrenoceptor agonists	a	a	1.000**	
Antimuscarinic bronchodilators	a	a	a	a
Corticosteroids	a	a		0.350
Cromoglicate & related therapy	a	a	0.527	
Leukotriene receptor antagonist	0.886		a	a

Therapeutic class in each body system	JORDAN		UK	
	correlation coefficient			
	positive	negative	positive	negative
Central nervous system				
Antipsychotic drugs	0.836		0.740**	
Antipsychotic 2nd generation drugs				0.216
Antimanic drugs	a	a	a	a
Tricyclic and related antidepressant	a	a	0.513	
Monoamine-oxidase inhibitors			0.896	
Selective serotonin reuptake inhibitors			0.624	
Other antidepressant drugs	0.780*		1.000**	
CNS stimulants and drugs used for attention defects hyper activity disorder	a	a	a	a
Drug used for obesity	a	a	a	a
Prophylaxis of migraine	a	a	0.685	
Control of epilepsies		0.446		0.575
Dopaminergic drugs	a	a	0.397	
Antimuscarinic drugs used in parkinosinosim	a	a		0.234
Drugs used in essential tremor , chorea, tics, and related disorders	a	a	a	a
Drugs for dementia	a	a	a	a
Endocrine system				
Sulphonylureas	0.333		0.618	
Other antidiabetic drugs	1.000**		a	a
Treatment of hypoglycaemia			a	a
Antithyroid drugs	a	a	a	a
Calcitonin and parathyroid hormones	a	a	a	a
Bisphosphonates & other drugs		0.098	1.000**	
Bromocriptine & other drugs	a	a	0.275	
Obstetrics, gynaecology and urinary-tract disorders				
Drugs for urinary retention		0.993**	0.552	
Drugs for urinary frequency	a	a		0.590
Malignant disease and immunosuppression				
Antiproliferative immune-suppressants	a	a	a	a
Other immunomodulating			a	a
Progestogens	a	a	a	a
Hormone antagonists	a	a	a	a
Gonadorelin analogues	0.498		0.832*	
Nutrition and blood				
Iron overload	a	a	a	a
Sickle cell disease			a	a
Carnitine deficiency			a	a
Nephropathic cystamine			a	a
Tyrosinaemia type_1			a	a

Therapeutic class in each body system	JORDAN		UK	
	correlation coefficient			
	positive	negative	positive	negative
Urea cycle disorders			a	a
Homocystinuria			a	a
Other metabolic disorder			a	a
Musculoskeletal and joint diseases				
Non-steroidal anti-inflammatory drugs		0.368	0.313	
Drug that suppress the rheumatic process	a	a	a	a
Long term control of gout			0.878**	
Enhance neuromuscular	a	a	a	a
Skeletal muscle relaxant	a	a		0.190
Eye				
Beta blocker		0.853**	0.926**	
Prostaglandin analogues	a	a	a	a
Carbonic anhydrase inhibitor	a	a	a	a
Sympathomimetic	a	a	a	a
Skin				
Preparation for psoriasis	a	a	a	a
Drug affecting immune response	a	a	a	a
Total				
Classes with correlation	15	7	27	14
Classes with significant correlation	6	2	10	1

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

a. Cannot be computed because at least one of the variables is constant

3.4.5 FACTORS IDENTIFIED FROM STUDYING THE CHANGE OF THE CARDIOVASCULAR SYSTEM'S DRUGS PRICES OVER TIME IN THE UK

3.4.5.1 EFFECT OF COMPETITION

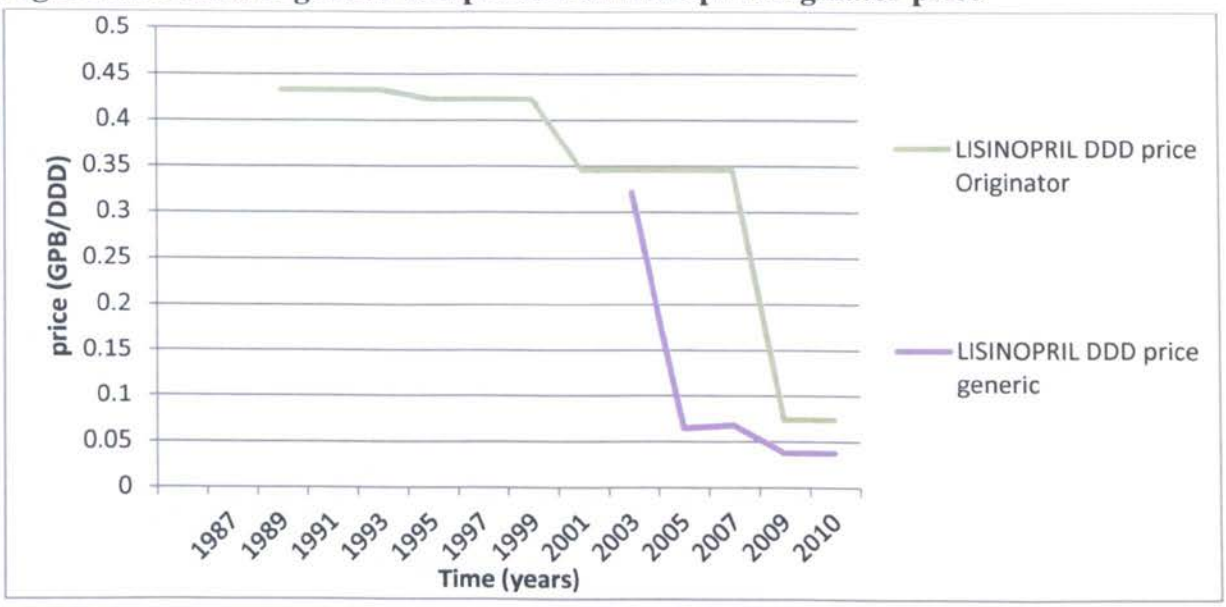
One of the factors that may influence the prices of originators is the competition posed by generic medicines as identified through previous research.[34, 39, 41, 51, 55,117,121,136] From studying the prices change over time for the cardiovascular medicines in the UK, there was a clear trend that when an originator drug reaches end of patency or at the launch of the equivalent generics, the price of that originator decreases.

The findings from this study were similar to the finding of a study conducted in Sweden in which the impact of actual and potential competition between originators and generics was studied based on 18 substances for the period from 1972 to 1996. The "potential competition" was considered as a situation where the originator's patent has expired but no generics have entered the market. Data analysis revealed that the price of the originator drug is lowered by both actual and potential generic competition.[153] Below is a summary of the trends observed in prices of medicines used within the cardiovascular system as a result of competition.

- **Own generic competition**

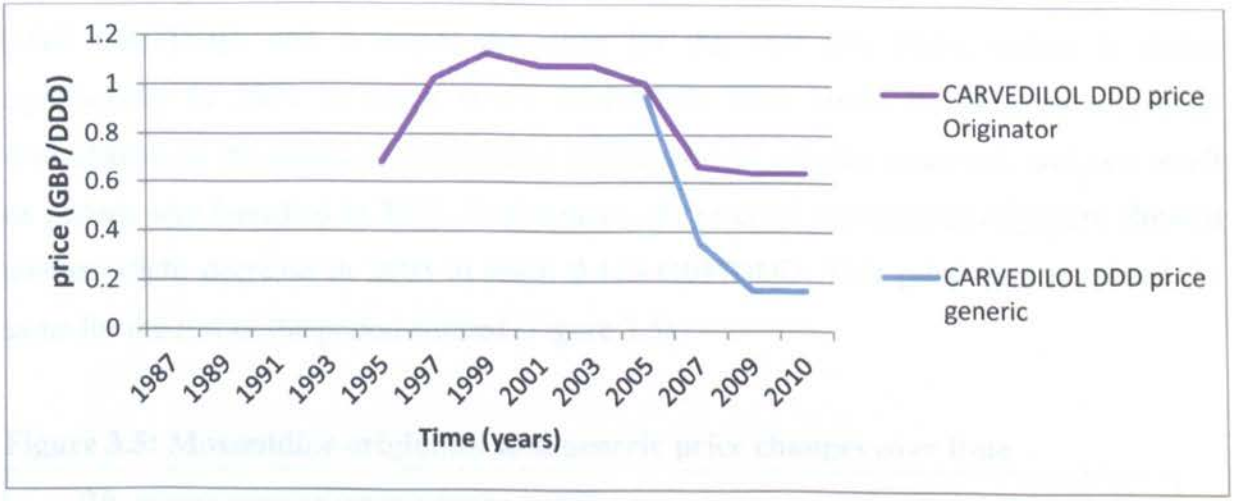
As seen in figure 3.2 below, lisinopril originator's price experienced a decline from 0.423 GBP/DDD to 0.346 GBP/DDD in 2001. This could be due to the fact that the patent of lisinopril originator was coming to an end (Figure 3.2). Lisinopril generic was launched in 2003. Furthermore, the price of lisinopril originator dropped dramatically from 0.346 GBP/DDD to 0.073 GBP/DDD in 2009 (79% decrease in price), when generics of other originators in the ACEIs class were launched (Figure 3.10). As shown in table 3.2, ACEIs had a negative significant correlation ($P<0.01$) between number of generics and mean price of originators ($r = -0.686$). This will be discussed further under competition with other generics in a class.

Figure 3.2: Effect of generic competition on lisinopril originator price



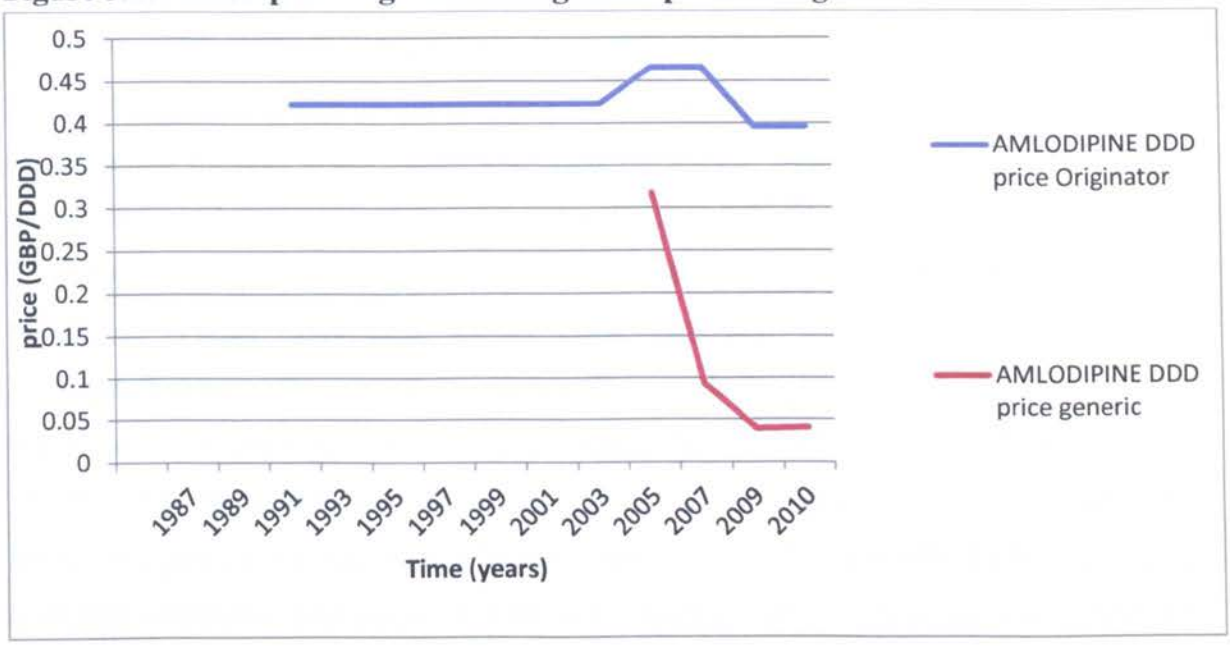
Similarly, the price of carvedilol originator (beta blocker) decreased from 1.002 GBP/DDD to 0.668 GBP/DDD (33.33% decrease) two years after its generic was first launched in 2005 (Figure 3.3).

Figure 3.3: Carvedilol originator and generic prices over time



The price amlodipine originator was reduced from 0.466 GBP/DDD in 2007 to 0.396 GBP/DDD in 2009 (15% decrease) after the substantial reduction of its generic's price to 0.09 GBP/DDD in 2007 from 0.318 GBP/DDD when it was first launched in 2005 (Figure 3.4).

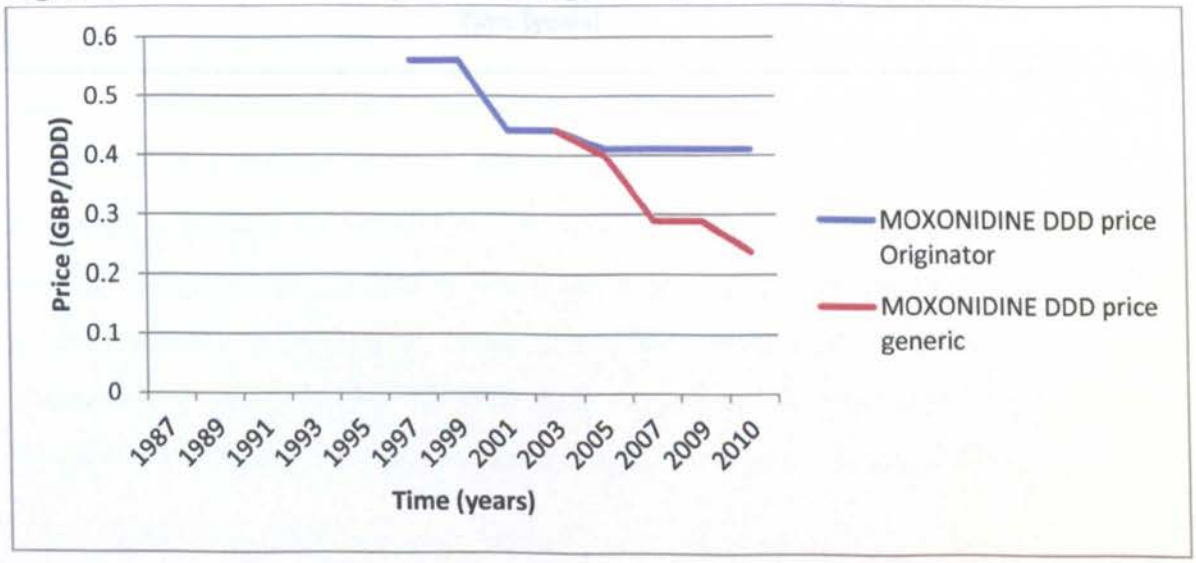
Figure 3.4: Amlodipine originator and generic price changes



In fact, CCBs showed a significant negative correlation between the mean price of originators and number of generics, with $r = -0.737$; $P<0.01$ respectively (Table 3.2).

The centrally-acting antihypertensive drug, moxonidine originator was launched in 1997 at 0.560 GBP/DDD, and it stayed the same for the next two years, before declining significantly in 2001 to reach 0.441 GBP/DDD. This could be seen as a generic competition, as the patent of moxonidine originator was coming to an end, and as a result its generic was launched in 2003. Furthermore, the price of moxonidine originator showed another slight decrease in 2005 to reach 0.410 GBP/DDD. This price then remained the same for the rest of the period studied (Figure 3.5).

Figure 3.5: Moxonidine originator and generic price changes over time



➢ **Generic paradox**

However, some individual originators from different classes showed an increase in their prices when their corresponding generics was launched such as, prazosin originator' price in the alpha blocker class which increased by 34.8% from 0.178 to 0.240 GBP/DDD (Figure 3.6) and quinapril originator's price (Figure 3.7) which increased by 19.9% from 0.768 to 0.921 GBP/DDD. Furthermore, the prices of amlodipine (Figure 3.4 above) and felodipine (Figure 3.8) from CCBs class increased by around 10% when their corresponding generics entered the market. This can be explained by the "generic paradox" phenomena discussed previously in this chapter and in detail in section 2.3.[40, 50, 51,53-55] It is interesting to note that the increase in originator price at time of generic launch allows the generic to launch at a higher price (Figures 3.7 and 3.8). However, whereas quinapril originator maintained a high price after its generic was launched, felodipine originator's price increased and its generic was launched at its same price and then their prices dropped consistently together from 0.319 GBP/DDD to 0.154 GBP/DDD, thus nullifying the saving from using a generic

Figure 3.6: Parazocin originator and generic prices over time

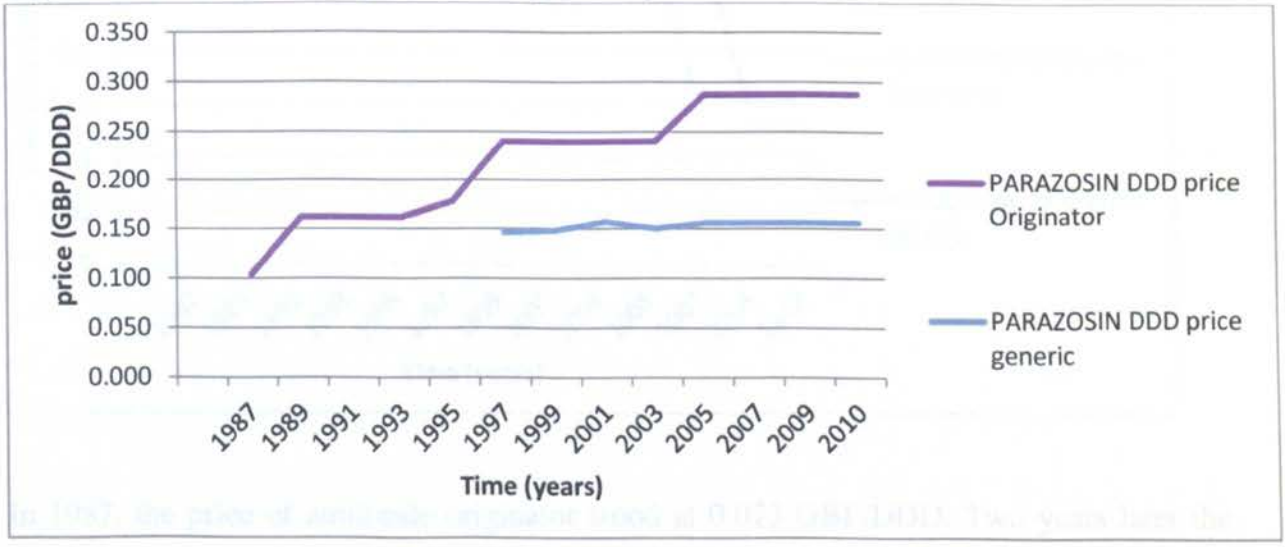


Figure 3.7: Quinalapril originator and generic prices over time

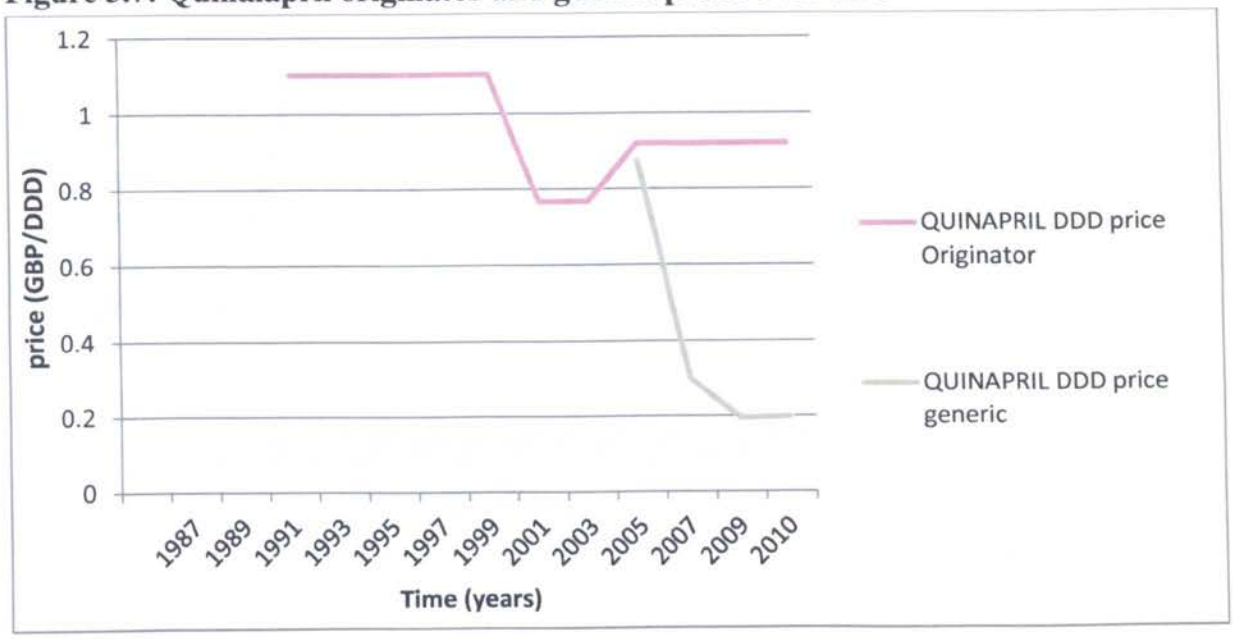
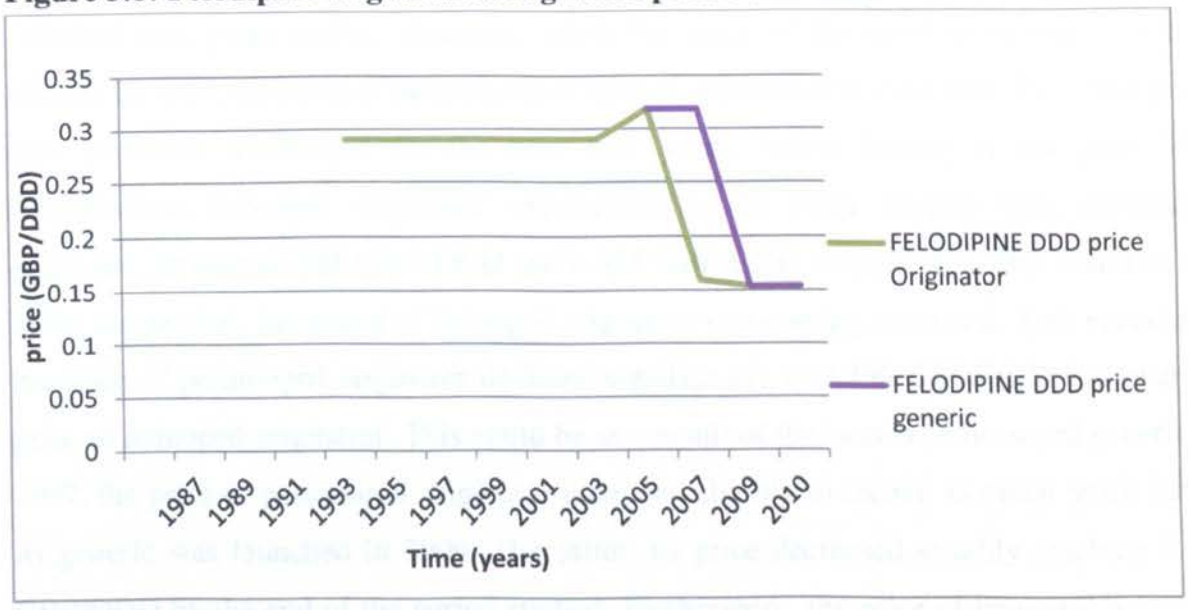
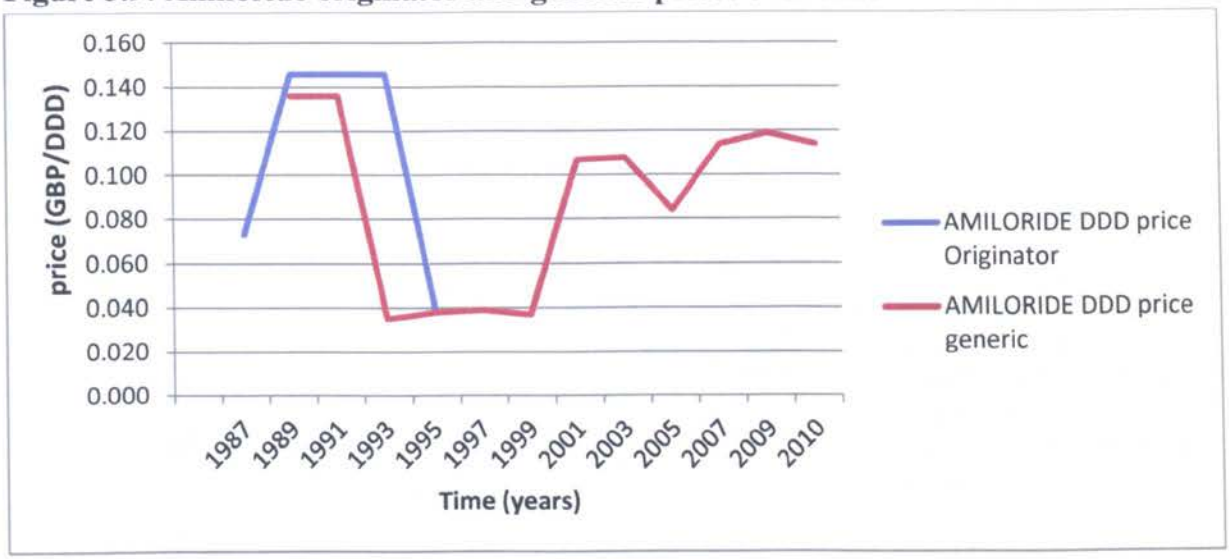


Figure 3.8: Felodipine originator and generic prices over time



In 1987, the price of amiloride originator stood at 0.073 GBP/DDD. Two years later the price of amiloride originator was doubled when its generic was launched in 1989, this could also be explained by the "generic paradox" phenomena (Figure 3.9). The price of amiloride originator decreased to 0.039 GBP/DDD in 1995 then it was discontinued. It is obvious that amiloride originator could not retain its market share while making enough profit to sustain its production, hence it was discontinued. Thus, generics entry promotes innovation as they remove the permanent monopoly on pharmaceutical products. This would encourage the originator companies to discover new medicines.[44]

Figure 3.9: Amiloride originator and generics prices over time

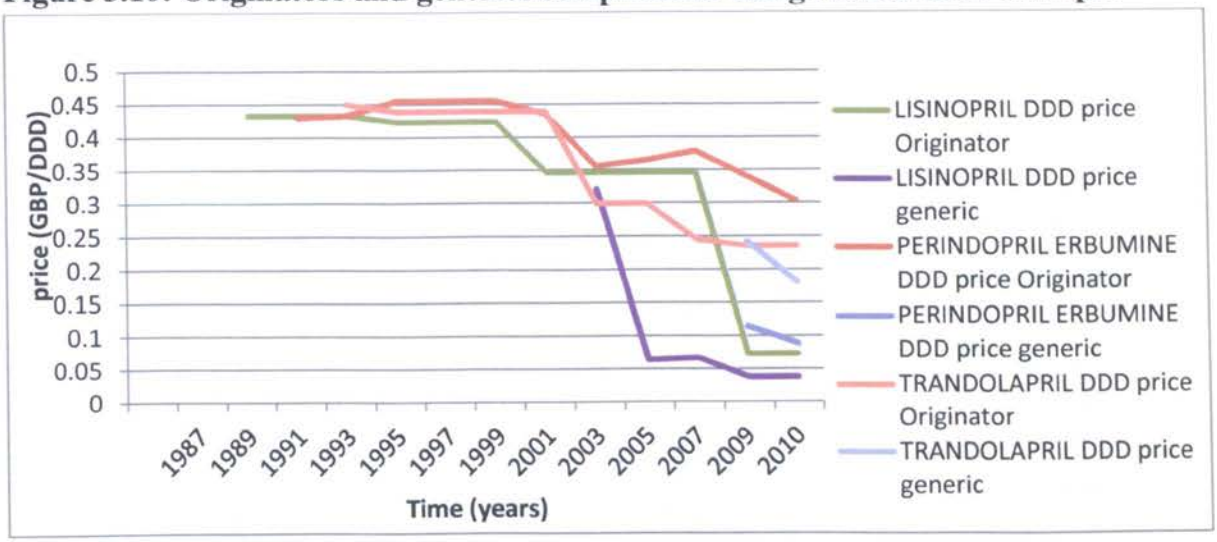


- **Competition with other generic in the class**

Perindopril originator was launched at same price of lisinopril originator, which was launched two years earlier. However, while the price of lisinopril originator decreased slightly in 1995, the price of perindopril originator increased by more than 5%. Both prices then remained unchanged for the next four years, before falling in the year 2001. Nevertheless, lisinopril originator experienced a far more decline than perindopril originator, to reach 0.346 GBP/DDD and 0.435 GBP/DDD respectively. This could be due to the reason that, the patent of lisinopril originator was coming to an end. Two years later, the price of perindopril originator declined significantly to 0.356 GBP/DDD just over the price of lisinopril originator. This could be as a result of the launch of lisinopril generic. In 2007, the price of perindopril originator increased slightly to recoup as much profit before its generic was launched in 2009. Thereafter, its price decreased steadily reaching 0.303 GBP/DDD by the end of the period studied. Furthermore, the price of lisinopril originator dropped dramatically in 2009, when generics of other originators were launched (Figure 3.10).

Moreover, the price of trandolapril originator remained the same since its launch in 1993 until the year 2001, before decreasing significantly in 2003 by almost 30% to reach 0.299 GBP/DDD. This could be seen due to a competition within the class, as lisinopril generic was launched in 2003. There was another decline in its price in 2007 to reach 0.245 GBP/DDD, as its patent was coming to an end. As a result the trandolapril generic was launched in 2009, when the price of trandolapril originator decreased further reaching 0.235 GBP/DDD by 2010 (Figure 3.10).

Figure 3.10: Originators and generics competitions using ACEIs as an example



- **Originator competition within class and "me too" drugs**

Another trend that was evident form the findings and consistent with previous research, is that the "me-too" or imitative products were always launched at a lower price than their predecessors, leading to competition within the class. [118] This can be clearly seen in the statin class (Figure 3.11) and CCBs (Figure 3.12). In the statin class, the newer originators were always launched at a lower price than their predecessors. Simvastatin and pravastatin were launched in 1991 at 1.960 and 1.734 GBP/DDD respectively, followed by fluvastatin in 1995 at 1.596 GBP/DDD, then atorvastatin in 1997 at 1.093 GBP/DDD. Finally, rousvastatin was launched at 0.644 GBP/DDD in 2003 (Figure 3.11).

In CCBs class, isradipine launched in 1989 at 0.696 GBP/DDD, then in 1991 amlodipine was launched at 0.423 GBP/DDD and felodipine was launched in 1993 at 0.29 GBP/DDD (Figure 3.12).

These results agree with the significant negative correlation between the mean price of originators and number of originators in both statin and CCBs classes shown in table 3.1, with $r = -.978$; $P<0.01$ and $r = -0.631$; $P<0.05$ respectively.

Figure 3.11: Comparison between statin originators' prices (GBP/DDD) over time

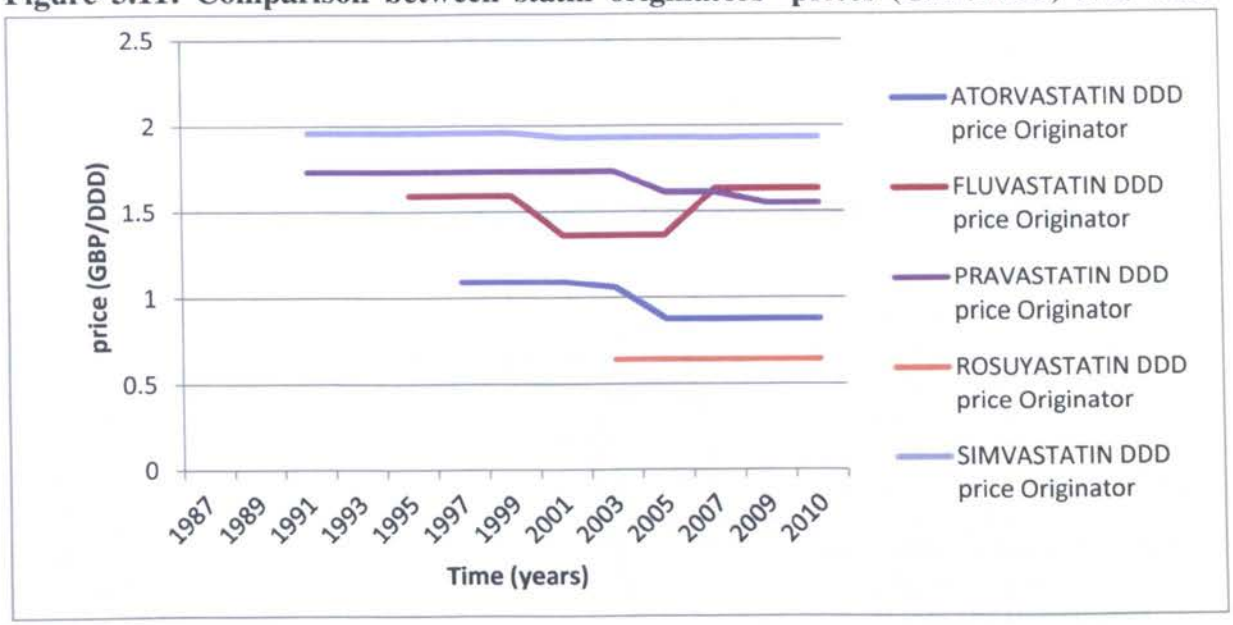
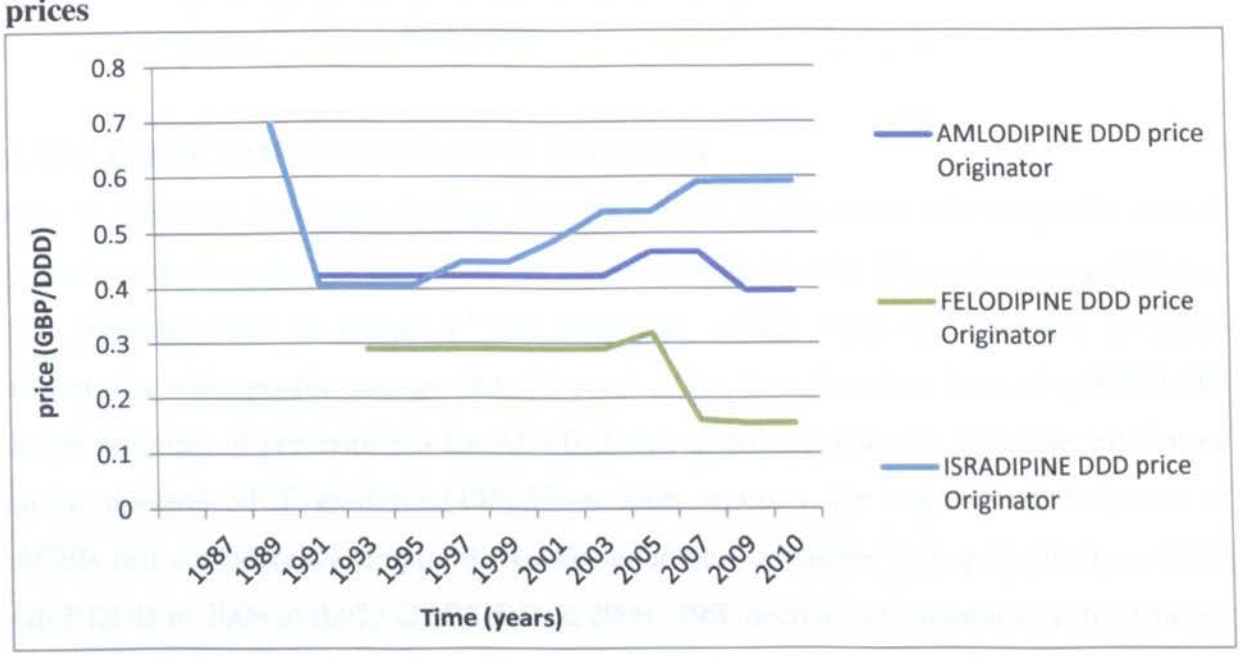


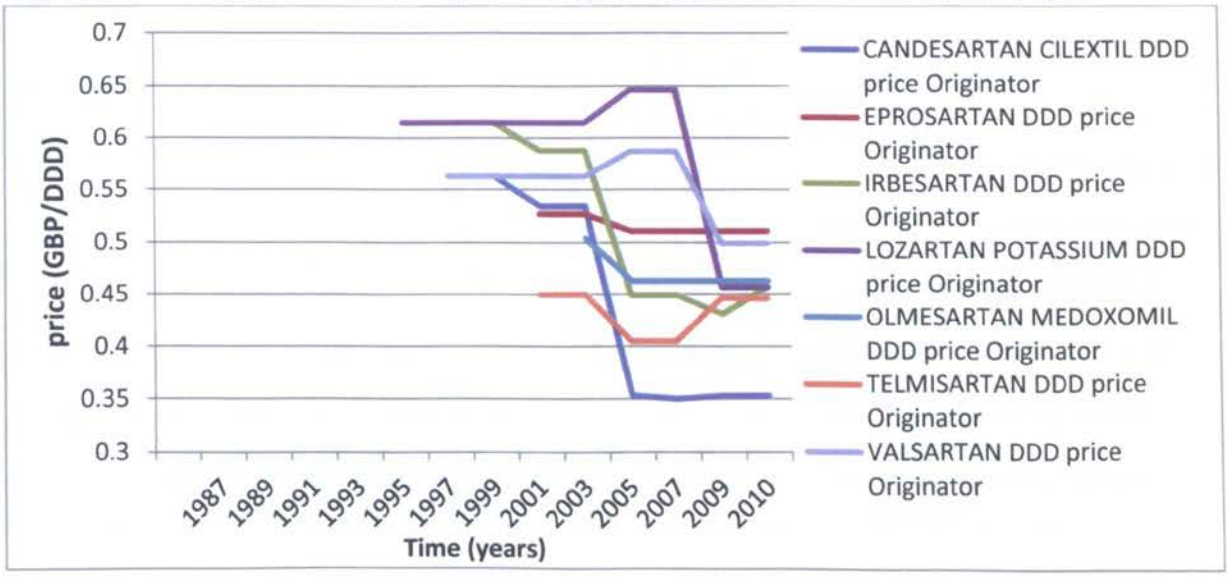
Figure 3.12: Comparison between CCB originators' prices (GBP/DDD) over time prices



Angiotensin II receptor antagonists also showed the same trend, as shown in figure 3.13. It can be clearly seen that, almost all the newer originators were either launched at the same or a lower price than their predecessors. Losartan was launched at 0.615 GBP/DDD in 1995 as the first drug in the class. Two year later valsartan was launched at a lower price of 0.563 GBP/DDD, it is interesting to note that irbesartan and candesartan launched at 0.563 GBP/DDD and 0.615 GBP/DDD to match the previous originators' price. However, after 6 years in the market, they immediately dropped their prices to sustain their market share. In fact, candesartan is the cheapest Angiotensin II receptor antagonist available. Telmisartan on the other hand, was launched in 2001 at a very low price (0.450

GBP/DDD) and its price kept decreasing until 2007. This can be explained penetration marketing strategy (see section 3.4.5.6), as the price of telmisartan was later increased in 2007 to match other originators within the class (Figure 3.13).

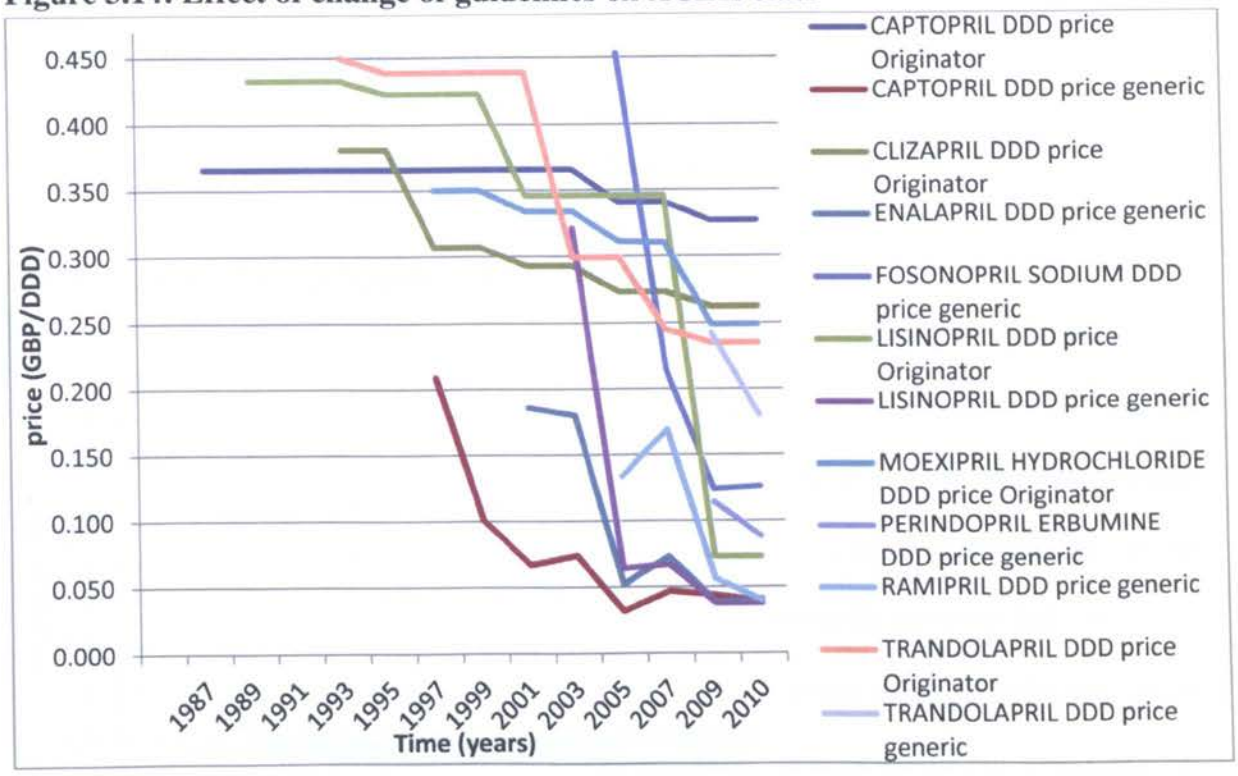
Figure 3.13: Angiotensin II receptor antagonists prices (GBP/DDD) over time



3.4.5.2 EFFECT OF CHANGE IN GUIDELINES

One of the most important findings from this study is the effect of changes in clinical guidelines on the prices of medicines. In 2006, according to NICE hypertension guidelines, beta blockers were no longer 1st line treatment, ACEIs were recommended as initial therapy for white people younger than 55 years. Since then, there has been an upward trend in the numbers of prescriptions for ACEIs drugs, consistent with the direction anticipated in the updated NICE guidance.[156] From 2006 onwards, the majority of the prices of ACEIs fell considerably (Figure 3.14). For example, originator lisinopril fell from 0.346 GBP/DDD in 2006 to 0.073 GBP/DDD in 2009 (79% decrease).Consequently the generics of lisinopril decreased by 43% in 2009 (from 0.067 to 0.038 GBP/DDD). This could be seen as a result of the increased demand due to the change in guidelines. The law of demand states that the quantity demanded and the prices of a commodity are inversely related.[157]

Figure 3.14: Effect of change of guidelines on ACEIs class



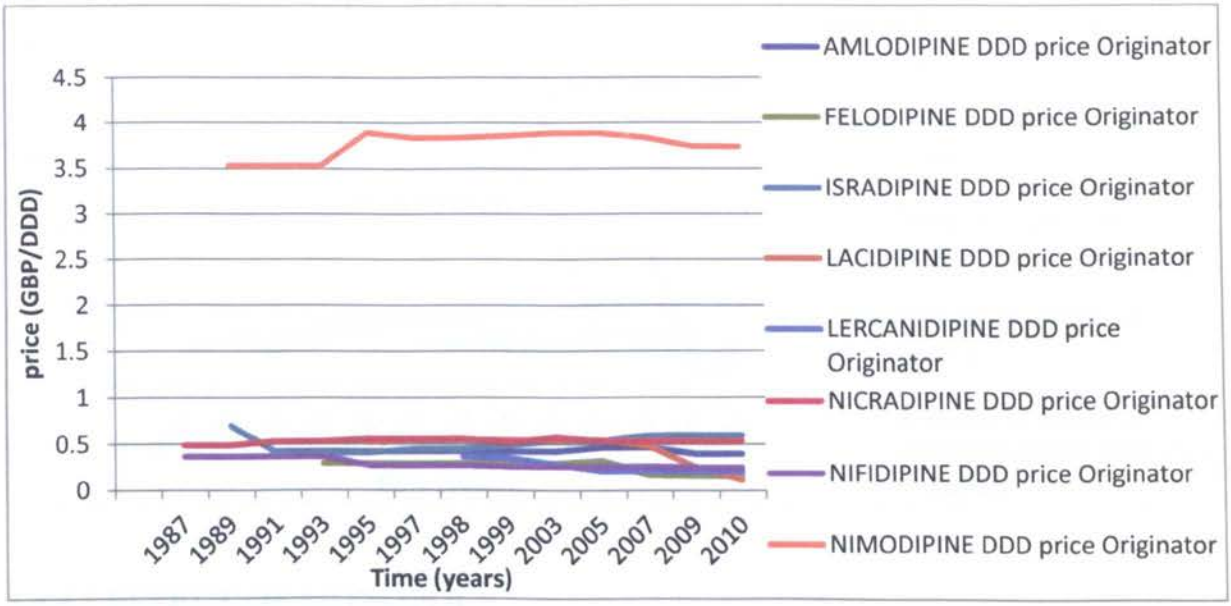
3.4.5.3 EFFECT OF CHANGE IN THERAPEUTIC USE/VALUE

Additionally, it was noted that when a new indication is identified for a drug, the price of that medicine increased. For example, carvidelol originator, was first launched at 0.682 GBP/DDD in 1995, then its price peaked at 1.127 GBP/DDD in 1999 when new indications (angina and heart failure) were added to its already existing indications (Figure 3.3).[158]

Moreover, clinical evidence may affect the prices of medicines. According to a randomised study, the anti-atherosclerotic effect of quinapril was found to be more potent than that of losartan in hypertensive patients.[159] This finding may have influenced the significant rise in its price in 2005. Furthermore, the price of nimodipine originator is much higher compared to the prices of all other originators throughout the studied period (Figure 3.15). This could be explained by the fact that nimodipine is the only CCB used for the prevention and treatment of ischemic neurological deficits following aneurysmal subarachnoid hemorrhage.[160] More therapeutically advanced drugs are likely to be accepted more rapidly due to their medical and scientific importance, with less need for introductory discounts or lower prices to promote market penetration and sustain their market share.[123]

In 1987, the prices of parazosin stood at 0.104 GBP/DDD. Two years later, the price of parazosin increased significantly by more than 50% to reach 0.162 GBP/DDD and stayed the same for the next four years. This could be explained by the fact that a new indications was added to the drug (Treatment of Raynaud's syndrome) (Figure 3.6).[161-162]

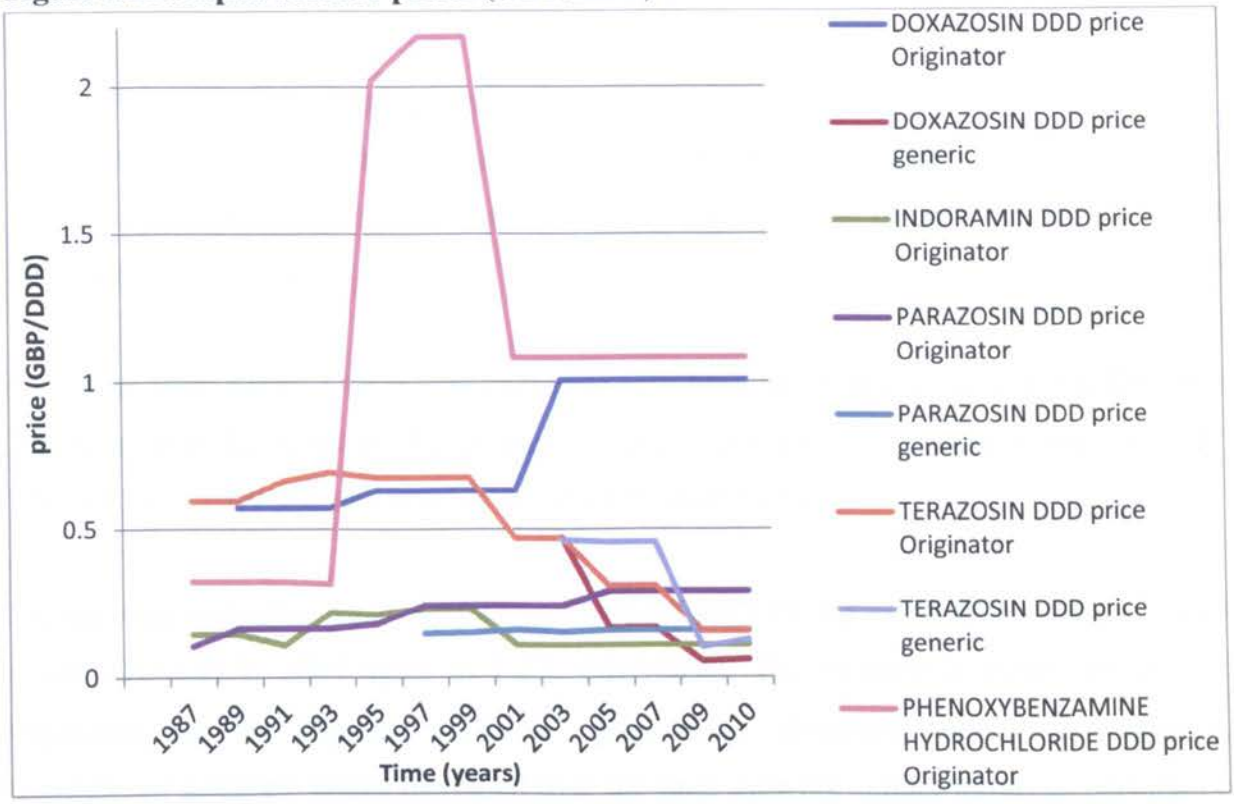
Figure 3.15: CCBs originators' prices over time



3.4.5.4 EFFECT OF DISEASE PREVALENCE

It is believed that the prevalence of a disease could be a factor that affects medicine prices. Drugs used for rare conditions can acquire a high price. The alpha blocker, phenoxybenzamine, is used for hypertensive episodes in phaeochromocytoma.[163] This very rare disease has a reported annual incidence in Europe of 2.1 cases per million population.[164] This could explain the high price of phenoxybenzamine (1.08 GBP/DDD) compared to the other alpha blockers as all of them are used for the same indications (Figure 3.16). The price of a drug is officially based on some determination of its therapeutic value and need/demands.[120,121] Furthermore, as explained earlier there is an inverse relation between demand and price, hence drugs for rare conditions are priced higher.[157]

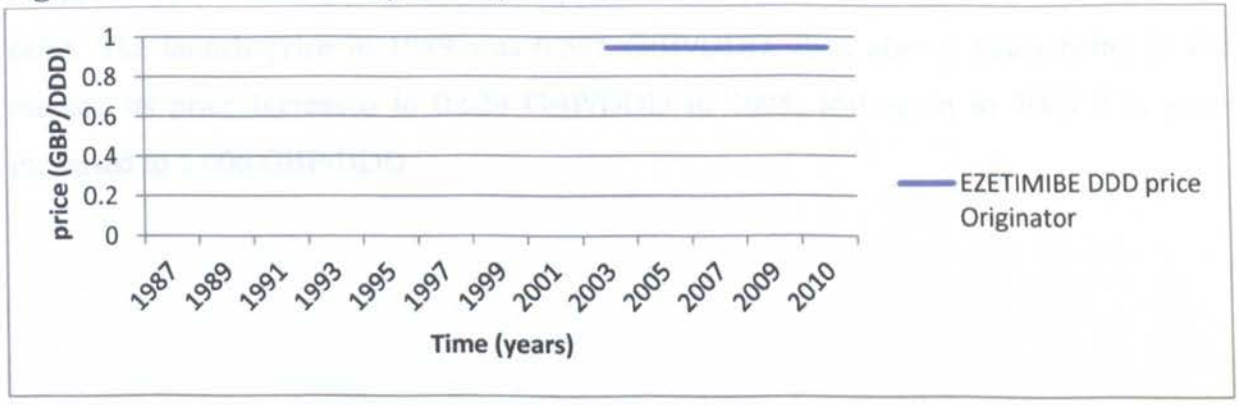
Figure 3.16: Alpha blocker prices (GBP/DDD) over time



3.4.5.5 EFFECT OF MONOPOLY

Ezetemibe originator is licensed as adjunct therapy for hypercholesterolemia with no competition, thus its price did not change since it was launched in 2003 at 0.940 GBP/DDD (Figure 3.17).

Figure 3.17: Ezetemibe originator price over time



3.4.5.6 EFFECT OF MARKETING STRATEGY

- **Penetration marketing strategy**

Penetration marketing strategy was shown in many classes such as; potassium sparing diuretics particularly triamterene originator drug (figure 3.18), fibrates (Figure 3.19) and doxazosin (Figure 3.20).

It is clear from figure 3.18 that triameterene was launched at low price 0.124 GBP/DDD and then after 12 years in the market, its price increased more than 9 fold to 1.127 GBP/DDD in 1999 and remained at that price (Figure 3.18).

Gemfibrozil originator price in 1987 was 0.96 GBP/DDD and increased in 1993 to 1.058 GBP/DDD and in 2005 again to 1.270 GBP/DDD. The increase in price can also be explained by the "generic paradox" phenomena discussed earlier. Interestingly, gemfibrozil generics' prices increased over the time showing similar trends of penetration strategy or this could be driven by the increase of gemfibrozil as a result of competition. Moreover cibrofibrate originator price showed an increase from 0.490 GBP/DDD at time of launch in 1993 to 0.631 in 2007 (increased by 28.8%) and stayed at that price (figure 3.19).

As seen from figure 3.20, since the launch of doxazosin in 1989 till 2003 (being in the market 14 years) doxazosin increased its price twice to achieve 76.4% more than its launch price. The launch price in 1989 was 0.571 GBP/DDD, then after 6 years being in the market, its price increased to 0.629 GBP/DDD in 1995, and again in 2003 it is price increased to 1.006 GBP/DDD.

Figure 3.18: Potassium sparing diuretics originator and generic prices over time

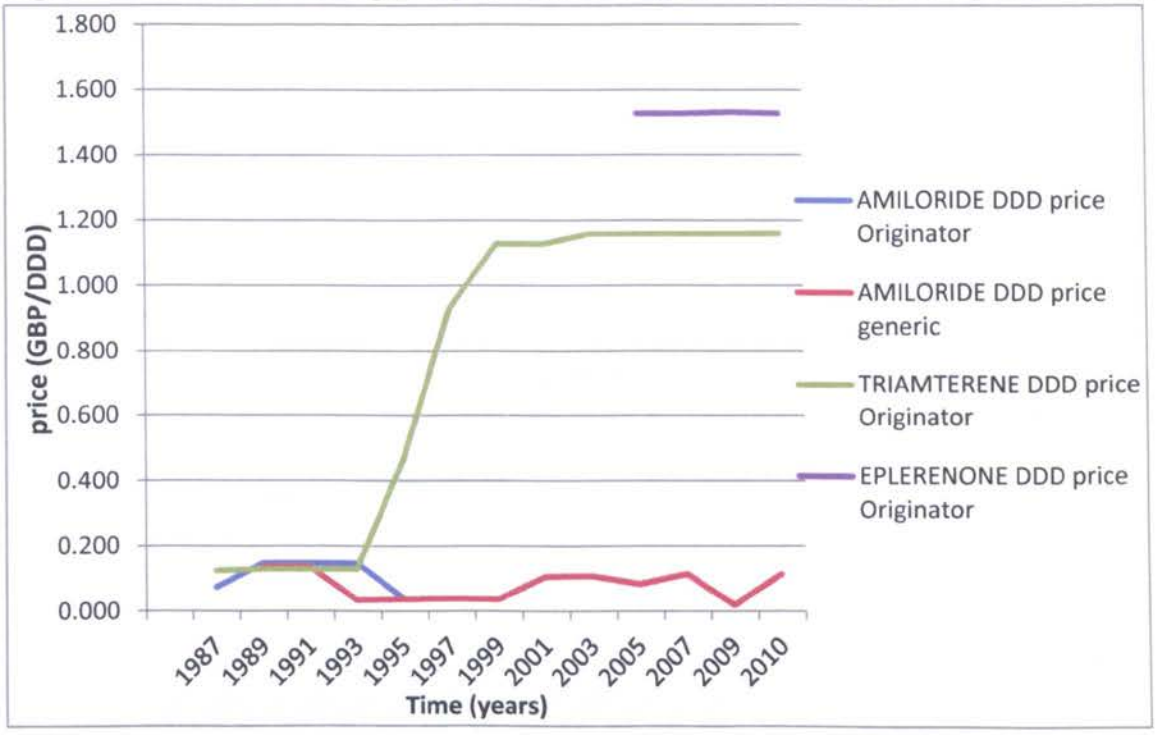


Figure 3.19: Fibrate price change over time

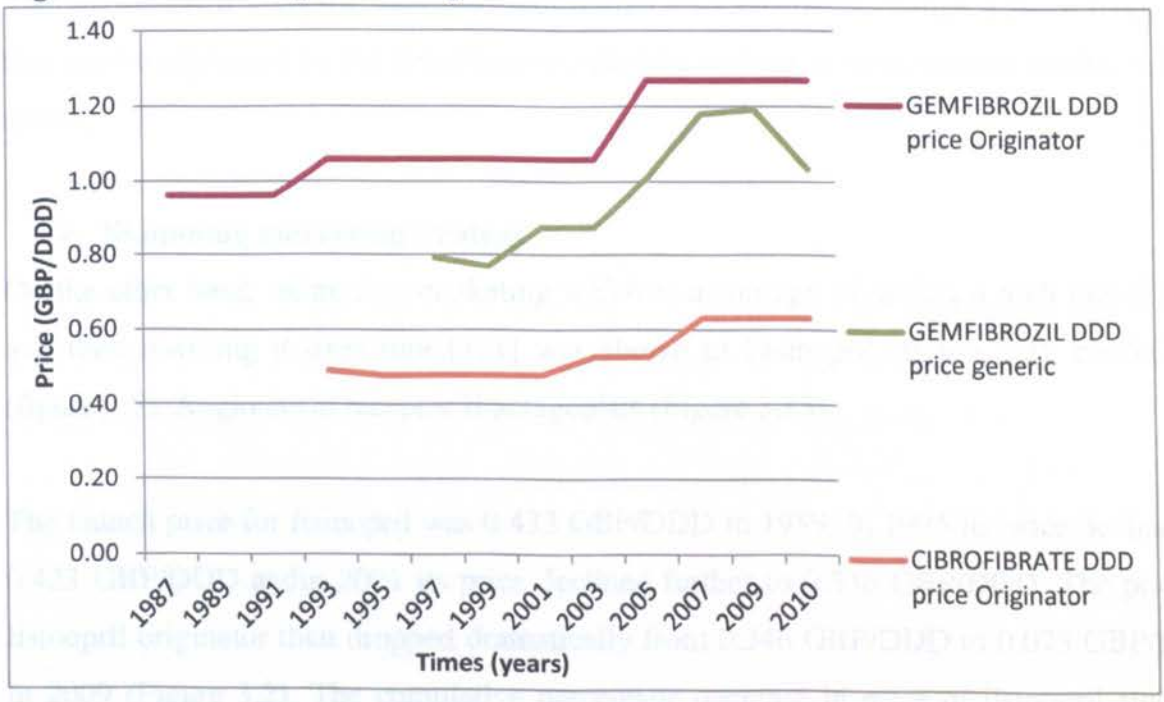
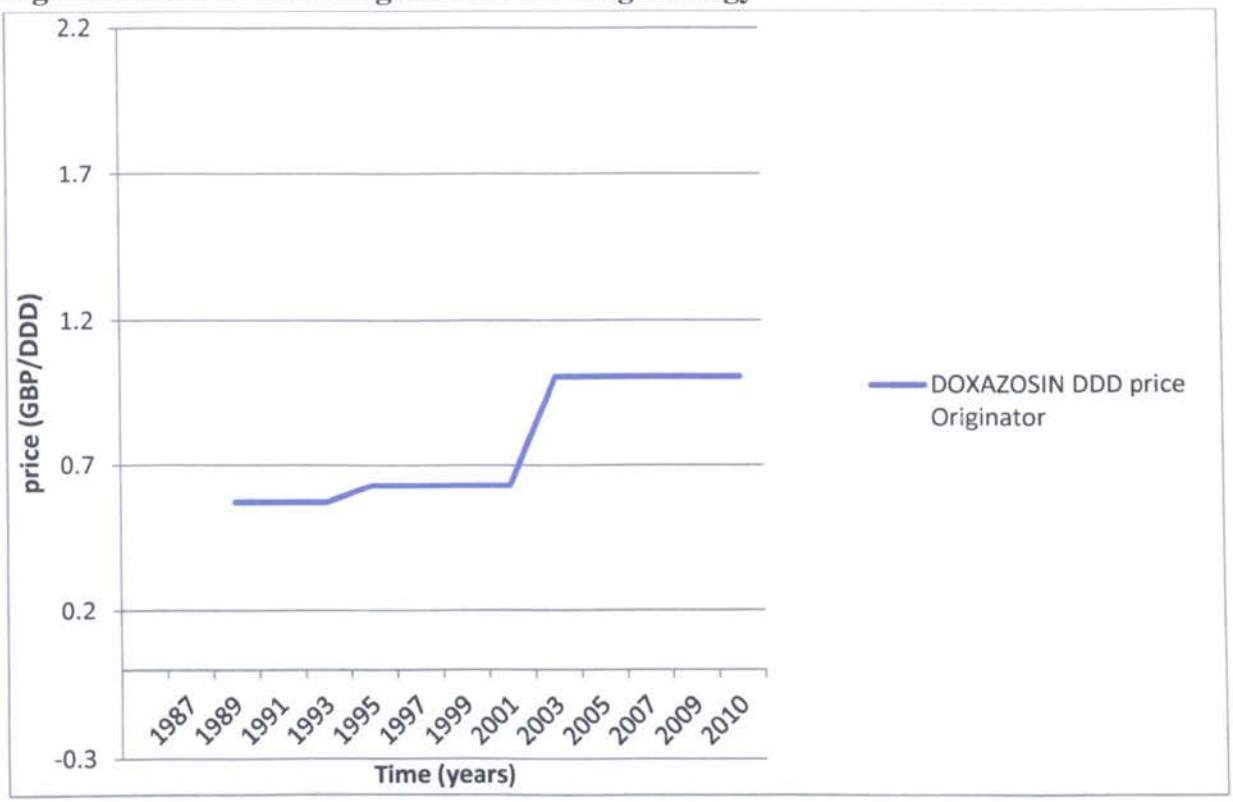


Figure 3.20: Doxazosin originator marketing strategy



The angiotesin II receptor inhibitor; telmisartan also showed a change a price over time that can be explained by the penetration marketing strategy as explained in section 3.4.5.1 above.

- **Skimming marketing strategy**

On the other hand, skimming marketing which is a strategy of setting a high initial price and then lowering it over time,[121] was shown in Lisinopril (figure 3.2), moxinidine (figure 3.5), Angiotensin receptor II antagonists (Figure 3.13).

The launch price for lisinopril was 0.433 GBP/DDD in 1989. In 1995 its price declined to 0.423 GBP/DDD andin 2001 its price declined further to 0.346 GBP/DDD. The price of lisinopril originator then dropped dramatically from 0.346 GBP/DDD to 0.073 GBP/DDD in 2009 (Figure 3.2). The cumulative percentage decrease in price of lisinopril since its launch till 2009 was 83.14%. Although, this could be partly explained by competition as discussed earlier in section in 3.4.5.1, this could also be seen as a skimming marketing strategy by setting a high initial price and reducing it over time.[121]

Other examples on skimming marketing strategy could be seen in the price changes of moxonidine originator over time. Moxinidine was launched at 0.560 GBP/DDD in 1997,

and then it declined to 0.441GBP/DDD in 2001. Furthermore, the price of moxonidine originator showed another slight decrease in 2005 to reach 0.410 GBP/DDD. This price then remained the same for the rest of the period studied (Figure 3.5).

Many drugs in the angiotensin receptor II antagonist class (Figure 3.13) showed skimming marketing strategy. Candesartan launched at 0.563 in 1999, after 2 years in 2001 it decreased its price to 0.534 GBP/DDD, further reduction of price of candesartan was seen in 2005 to reach 0.353 GBP/DDD (a decrease of 37.3% of the launch price). Moreover, irbisartan launched in 1999 at 0.615 GBP/DDD and declined over time to reach 0.457 GBP/DDD in 2010.

3.4.5.7 INTERACTION OF VARIOUS FACTORS TO INFLUENCE THE PRICE OF MEDICINES IN THE UK

To summarise how various factors influence the pricing of drugs in the UK, drugs from the beta blockers class will be used as an example (Figure 3.21). Compulsory generic prescribing started in 1997 [165]; therefore, there was a slight or no influence of generic competition on the prices of originators before 1997. For instance, the patent of atenolol originator expired in 1989; however, its price stayed the same for the next 20 years at 0.187 GBP/DDD, when it dropped by almost half. This could be due to the change in guidelines (no longer 1st line treatment).[156] Another example is metoprolol, when the generic was first launched in 1989, the price of the originator increased steadily for 8 years from 0.140 to 0.275 GBP/DDD (penetration marketing strategy), before falling after the year 1999 to 0.138 GBP/DDD, and then it stayed the same till 2010. This may indicate the effect of compulsory generic prescribing (generic competition) (Figure 3.21).

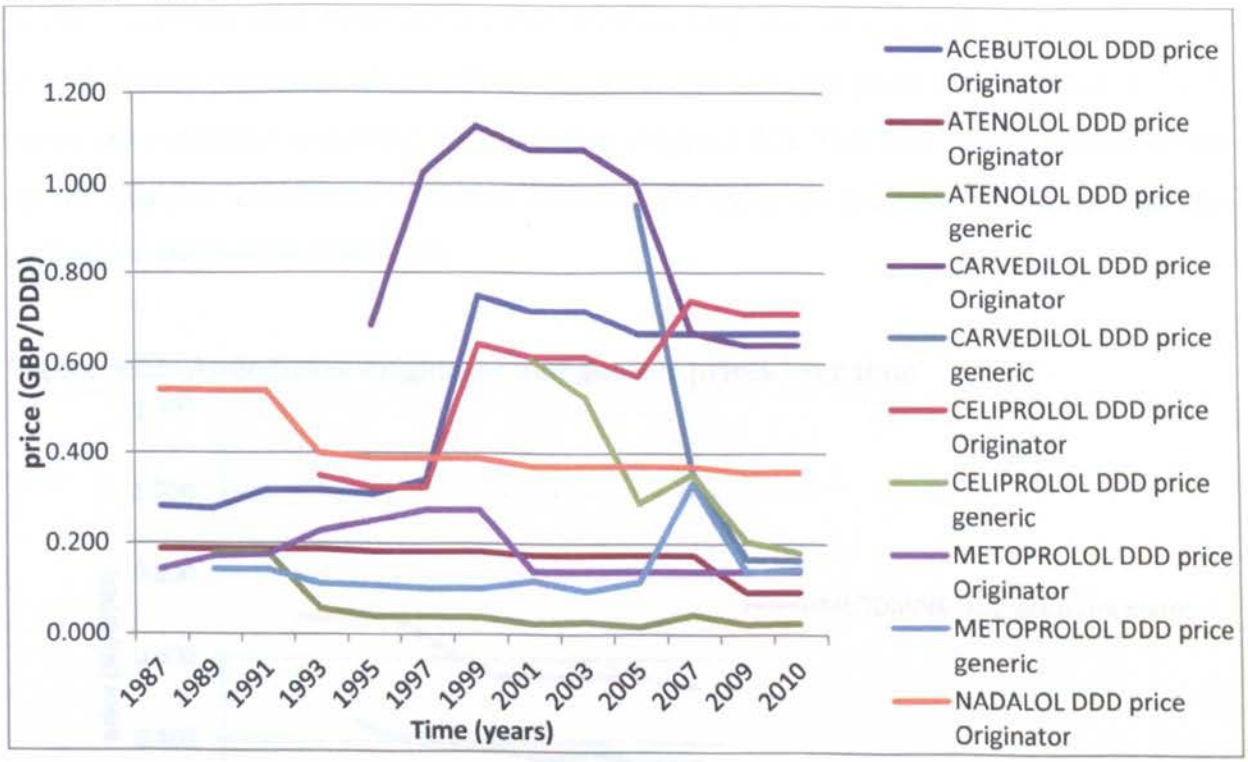
The price of celiprolol originator at launch matched the price of the other beta blockers. The price then increased in 1999 to more than 1.5 times, this might be due to penetration marketing strategy or it might be an attempt to make more profit before its generic is launched. In fact, when the generic was launched in 2001, celiprolol originator dropped its price slightly (generic competition) (Figure 3.21). Acebutolol doesn't have a generic but it follows the same trends of celiprolol originator.

As outlined above, not only does originator/generic competition has an effect on prices of originators, competition from other originators (within class competition) might also

influence a change in a price. For example, the price of nadalol dropped in 1993 from 0.539 to 0.339 GBP/DDD when celiprolol originator was launched (Figure 3.21)

Carvedilol originator was first launched in 1995 at 0.682 GBP/DDD, then its price peaked at 1.127 GBP/DDD in 1999. This could be due to the fact that new indications (angina and heart failure) were added to its already existing indications, so its therapeutic value increased. Four years before its generic was launched, the price of carvedilol originator started to fall slightly, this could be due to the competition from nebivolol originator (launched in 1999) and celiprolol generic (launched in 2001), so competition within the class. In 2005, the patent for carvedilol originator expired. This resulted in the availability of less expensive generic forms, which led to a dramatic decrease in the price of the originator from 1.002 to 0.668 (33.33% decrease) and then followed by slight reduction of 4% to 0.640 GBP/DDD (Figure 3.21).

Figure 3.21: Factors influencing prices of medicines over time in the UK, beta blockers example

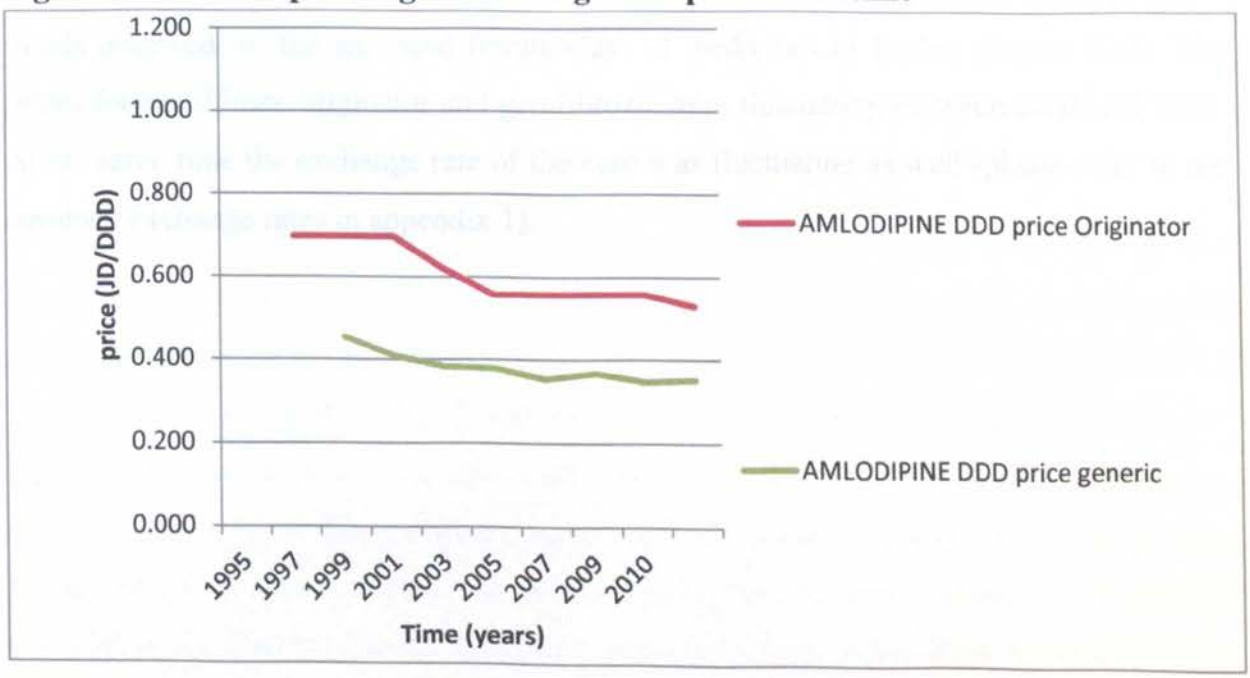


3.4.6 FACTORS IDENTIFIED FROM STUDYING THE CHANGE OF THE CARDIOVASCULAR SYSTEM'S DRUGS PRICES OVER TIME IN JORDAN

3.4.6.1 EFFECT OF THE PRICING POLICY

In Jordan, the pricing policy for generic medicines was found to be the main determining factor that affects their pricing. The pricing policy states that the requested price for a locally manufactured generic medicine should not exceed 80% of the price of its originator.[15] It was clearly seen that the price of most generics in Jordan was at least 20% less than their originator. The price of amlodipine originator in 1995 was 0.699 JD/DDD and it started decreasing since 2001 to reach 0.529 JD/DDD in 2010. The generic version of amlodipine was launched in 1997 at 0.453 JD/DDD (35% cheaper than the originator) and the average price decreased to reach 0.351 JD/DDD. This decrease could be due to the fact that the price calculated is the average price of all generics available and as the number of generics increase the competition increases with the new generics being priced lower than their predecessors. The decrease may also be due to the drop in the price of amlodipine originator which affects the mean price of the generic amlodipine as both prices are correlated as per the pricing policy (Figure3.22). This was further demonstrated by the positive correlation observed between the price of generics in Jordan and the equivalent originators (Table 3.4)

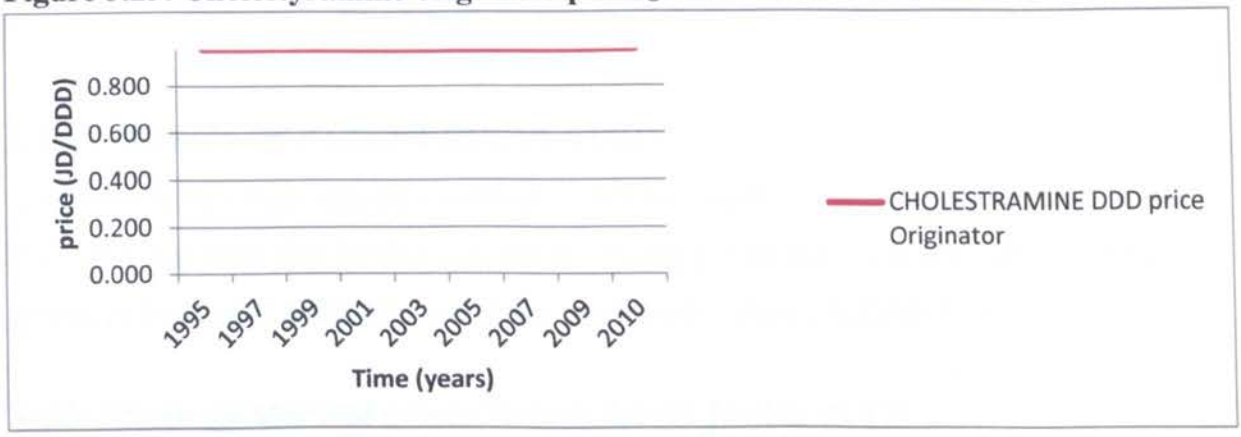
Figure 3.22: Amlodipine originator and generic prices over time



3.4.6.2 EFFECT OF MONOPOLY

Similar to UK, another interesting finding identified from the study is that the price of drugs which are singly available in a class (monopolising the market) such as ezetemibe which stayed at the same price throughout the period studied. The lack of competition could explain this finding. Another example is cholestyramine originator; a bile acid sequestrant. Cholestyramine hydrochloride is the only available bile acid sequestrant in Jordan (Figure 3.22). The price of cholestyramine originator stayed the same for the whole period from 1995-2010 at 0.957 JD/DDD (Figure 3.23).

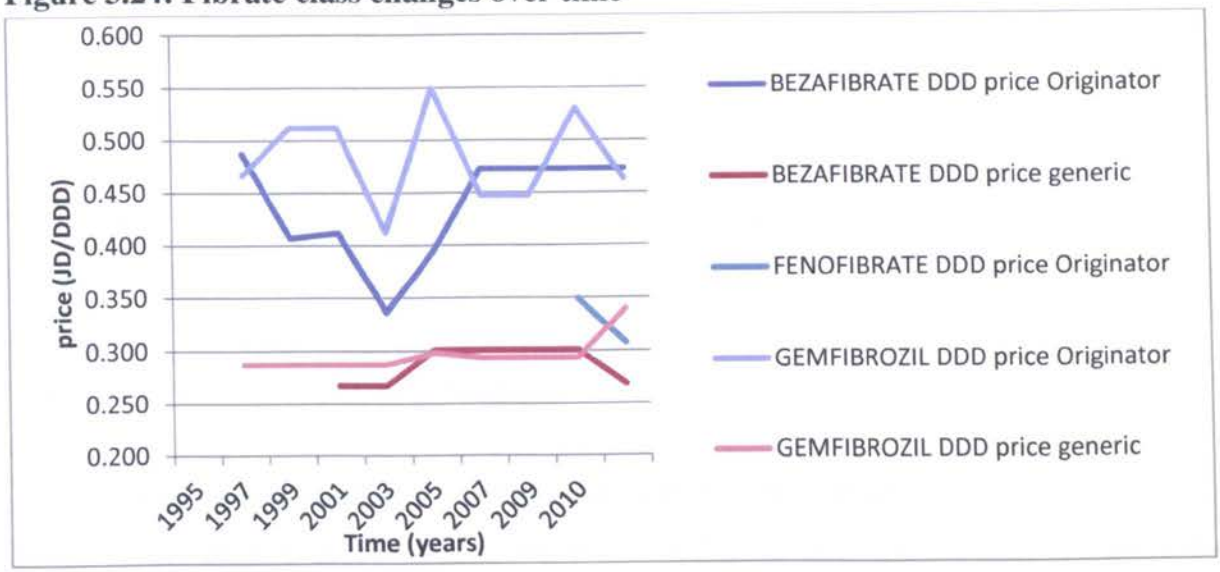
Figure 3.23: Cholestyramine originator price JD/DDD over time



3.4.6.3 EFFECT OF EXCHANGE RATE

In Jordan, all originators are imported, thus the currency fluctuation was noticed to be a factor affecting originator drug prices. This was consistent with previous research which found that the exchange rate influence the prices of medicines.[139] This might explain the trends observed in the anti-lipid fibrate class of medicines in Jordan (Figure 3.24). The prices for bezafibrate originator and gemfibrozil were fluctuating between 2001 and 2005. At the same time the exchange rate of the euro was fluctuating as well (please refer to the currency exchange rates in appendix 1).

Figure 3.24: Fibrate class changes over time



3.4.6.4 EFFECT OF PATENT REGULATION

It was noted that some generics were available in Jordan at a much earlier date than in the UK. This indicates that Jordan was not following patent law as generic drugs should not appear in the market before the originator patency has expired (Table 3.5).

Table 3.5: Originator and generic launch date in Jordan vs. UK

Drug name	Date originator launched		Date first generic launched	
	Jordan	UK	Jordan	UK
Simvastatin	1991	1989	1997	2004
Enalapril	1987	1985	1989	2000
Lisinopril	1991	1988	1994	2003

Jordan became a member of the World Trade Organisation (WTO) in 2000.[166] Under the WTO arrangements, countries have to recognise product protection throughout the patent period which is normally 20 years, half of which is usually taken up in product R&D. Jordan also signed a Free Trade Agreement (FTA) with the USA in the same year, the FTA provides protection for trademarks, copyrights and patents with specific attention to pharmaceuticals, as patents are especially prone to violation.[167] As part of its trade commitments, Jordan accepted the World Intellectual Property Organization (WIPO) Copyrights and Patents Treaty, this came into effect from April 2004 resulting in new patency regulations in Jordan.[168] Prior to signing up the WTO agreement, local

companies in Jordan were able to produce generics' equivalents of new drugs before patent expiration. However, the WTO agreement has put a stop to this. As a result for not applying the patency regulations in Jordan before 2004, many generics of the studied drugs were launched in the Jordanian market before the launch of their originators. Thus identifying the effect of the launch of generics on the prices of originators was immeasurable.

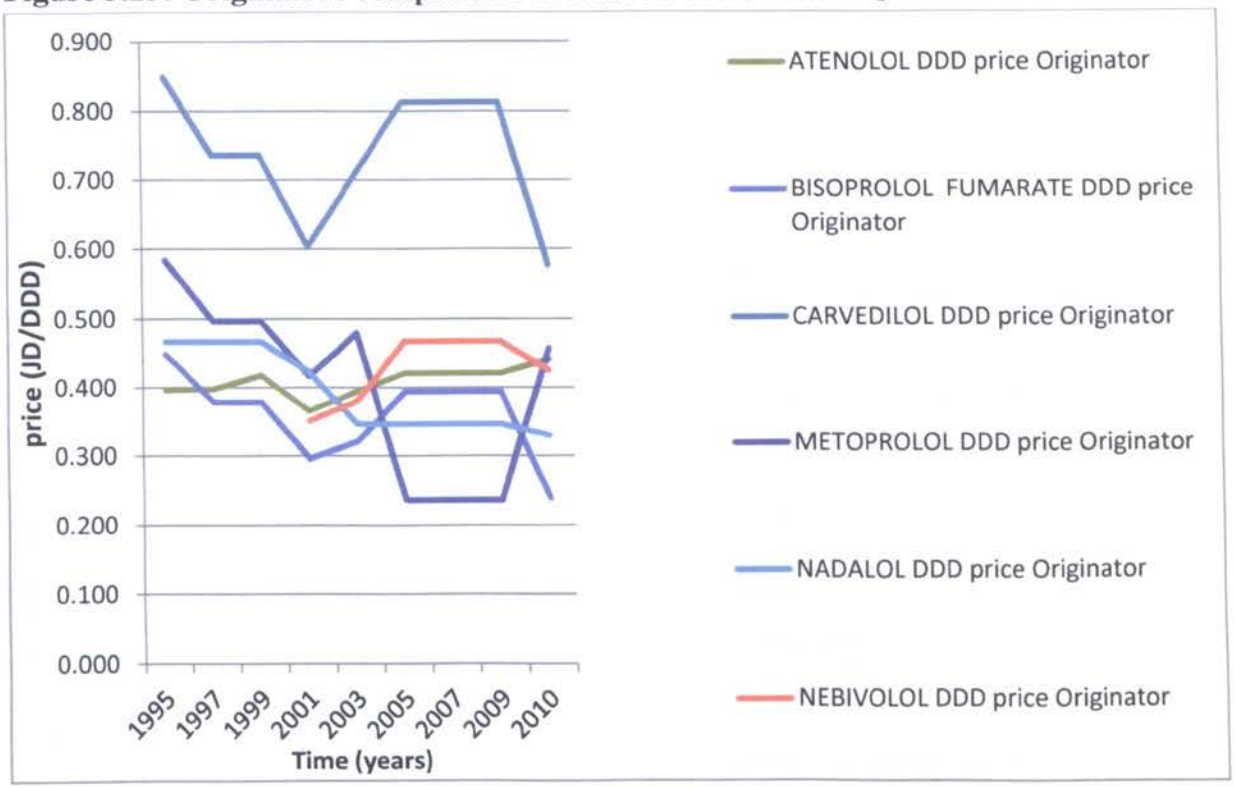
3.4.6.5 EFFECT OF COMPETITION

- **Originator competition within class and "me too" drugs**

Seven of the studied beta blockers originator medicines were available in Jordan in the year 1995. However, nebivolol originator was launched at a price of 0.351 JD/DDD in 2001. This could have been the reason why the prices of carvedilol, atenolol, bisoprolol, nadalol and metoprolol originators fell considerably in the same year. This could be explained by competition between drugs within the same class (Figure 3.25). It is interesting that nebivolol price then increased in 2003 to match the other originators within the class, this could be seen as a penetration marketing strategy to ensure market share.

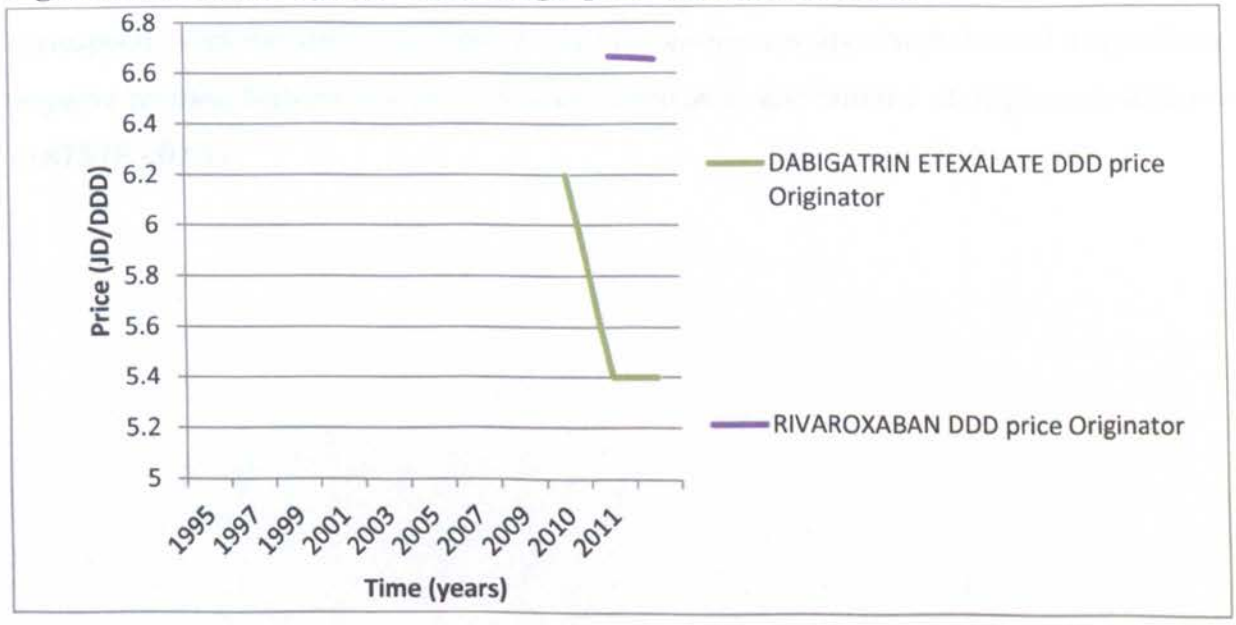
Parallel to the UK, carvidelol originator price peaked in 2001 when new indications (angina and heart failure) were added to its already existing indications (Figure 3.25).[158] Thus, the change in international guidelines and therapeutic value also has an influence on the prices of drugs in Jordan. This reflects the pricing policy which uses reference pricing.[117]

Figure 3.25: Originators competition in beta blockers class in Jordan



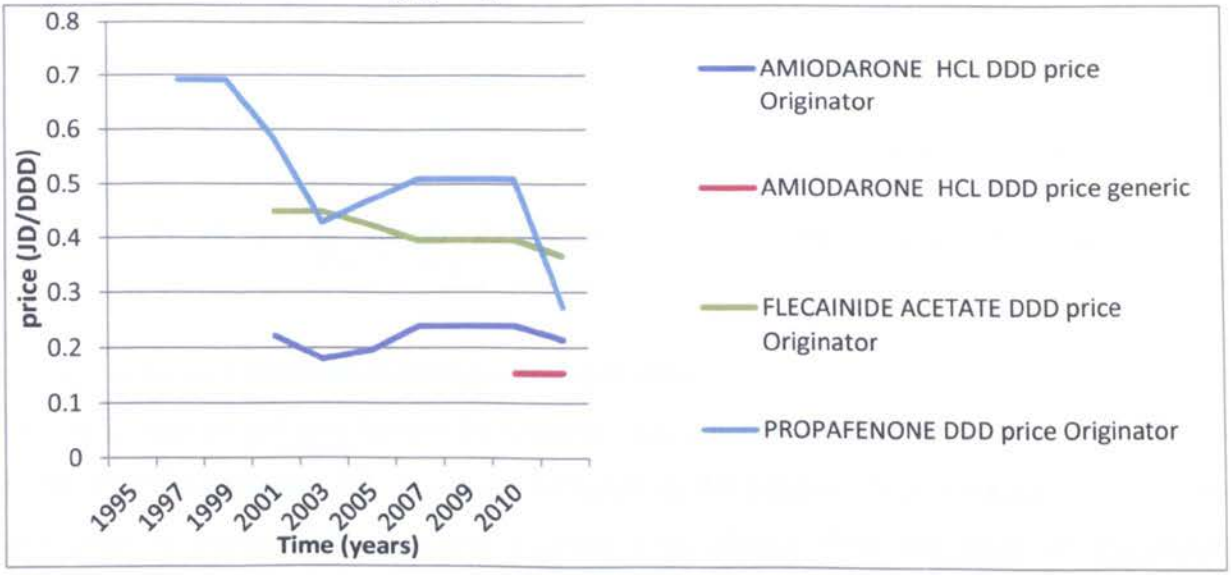
Another example for competition between originators in the class is the anti-coagulant dabigatran etexilate. Dabigatran originator was launched at 6.199 JD/DDD then its price declined to 5.399 JD/DDD when rivaroxaban originator was launched in 2010 at 6.665 JD/DDD (Figure 3.26).

Figure 3.26: Anti-coagulant class drugs' price change in Jordan



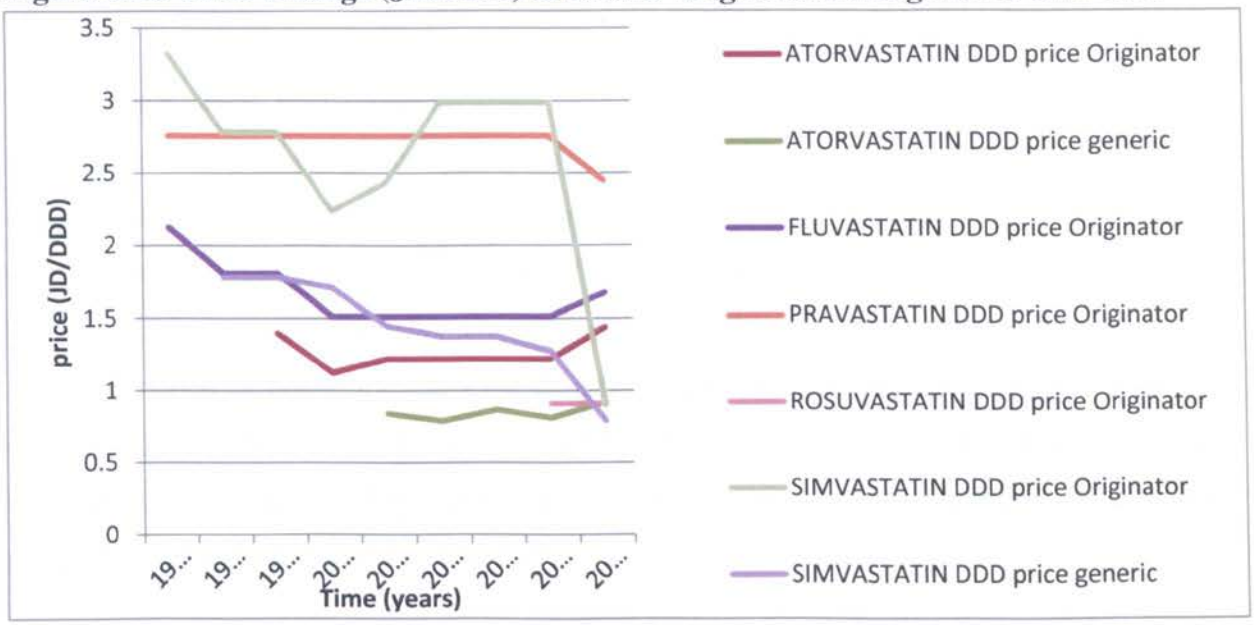
Furthermore, propafenone originator was the only anti-arrhythmic drug available in Jordan in 1995, it was selling at 0.691 JD/DDD. However, its price decreased in 1999 when two new originators entered the market; amiodarone originator and flecanide originator, to 0.583 JD/DDD (15.63% decrease) (Figure 3.27).

Figure 3.27: Comparison between originator and generic prices JD/DDD over time for the anti-arrhythmic drug group



Originator competition was seen within the "Me too" drugs in Jordan similar to the trends observed in the UK. As seen in the statin class in Jordan (Figure 3.28), atorvastatin originator was launched in 1999 at a lower price than other statin predecessors already in the market. Furthermore, rosuvastatin was launched in 2009 at 0.911 GBP. This corresponds with the statistical Pearson correlations test results which showed a significant negative relation between the price of statin originators and number of originators with $r = -0.875$ ($P < 0.01$).

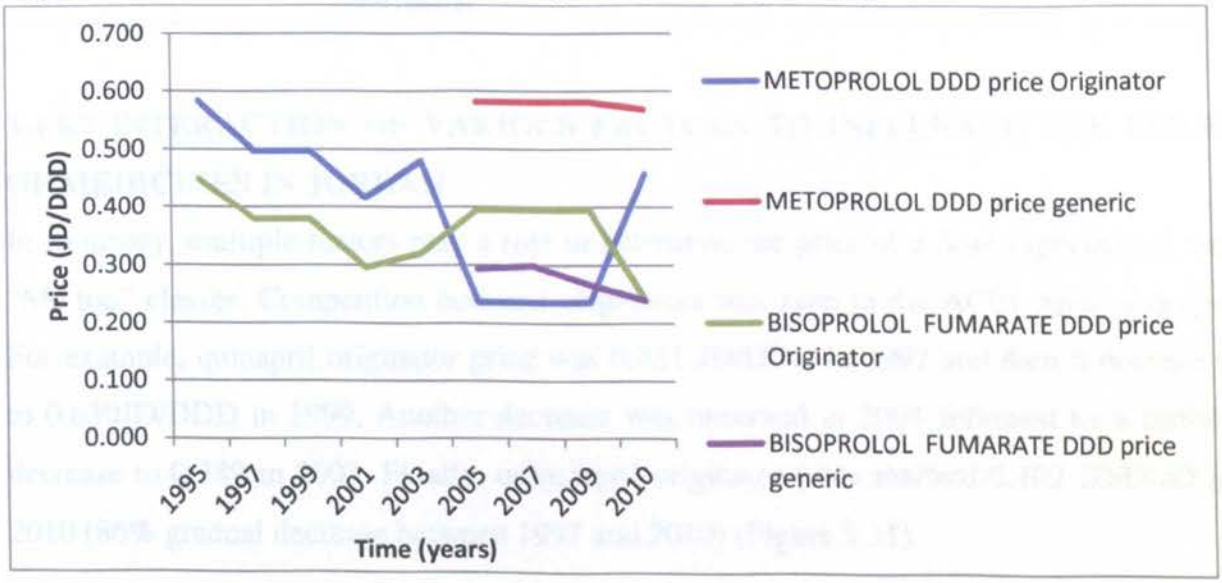
Figure 3.28: Price Change (JD/DDD) of statins' originators and generics over time



- **Generic competition and generic paradox**

In 2005, metoprolol and bisoprolol generics were both launched at 0.582 JD/DDD and 0.294 JD/DDD respectively. This was reflected in the prices of their originators. Whereas the price of metoprolol originator decreased by almost 50% the price of bisoprolol originator showed a slight increase. This could be explained by generic/originator competition in the metoprolol case, and the "generic paradox" phenomena in bisoprolol case (Figure 3.29).

Figure 3.29: Beta blockers generic competition and "generic paradox" in Jordan

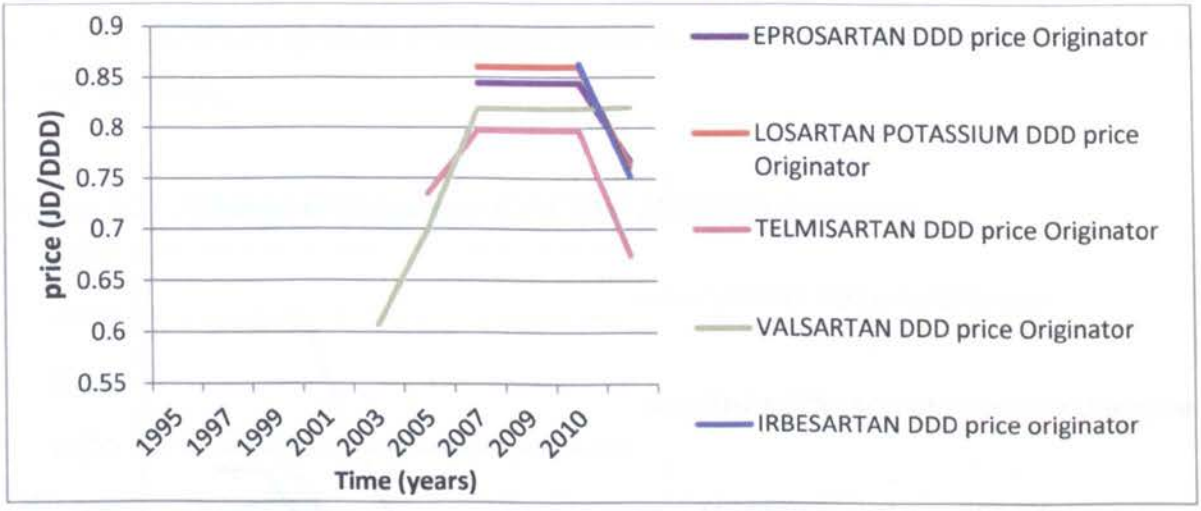


3.4.6.6 EFFECT OF MARKETING STRATEGY

- **Penetration marketing strategy**

The penetration marketing strategy was seen in some classes of drugs such as angiotensin receptor inhibitors. Valsartan originator was launched in 2001 at a price of 0.607 JD/DDD, its price was increased to 0.699 in 2003. Then, in 2005 its price was increased again to 0.819 (34.9% increase since launch) (Figure 3.30). The increase in price was maybe to match the price of other originators within the class. However, whereas other originators dropped their prices in 2010 due to competition to ensure market share, valsartan originator maintained its high price, as it secured customers'/prescribers' loyalty and preference through its lower launch price.

Figure 3.30: Penetration marketing strategy using valsartan originator as an example



3.4.6.7 INTERACTION OF VARIOUS FACTORS TO INFLUENCE THE PRICE OF MEDICINES IN JORDAN

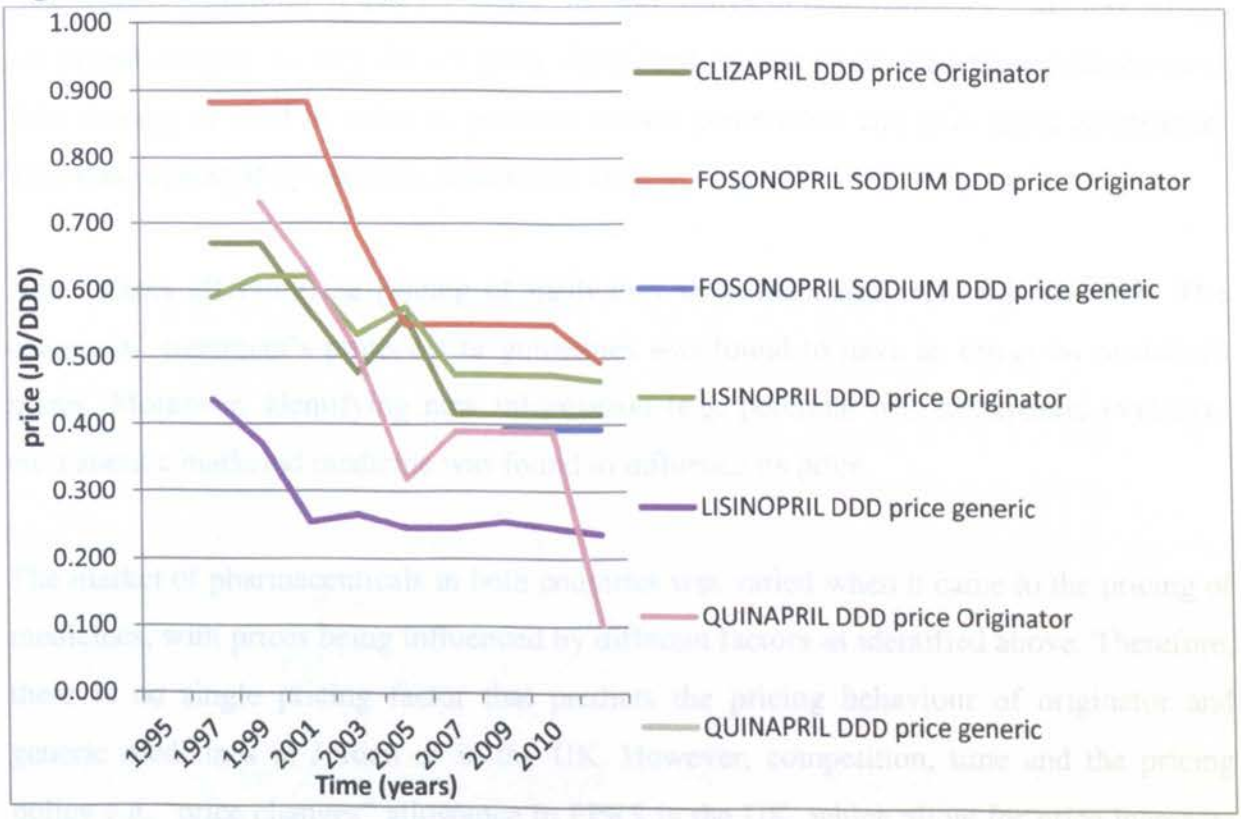
In summary, multiple factors play a role to determine the price of a drug especially in the "Me too" classes. Competition between originators was seen in the ACEI class of drugs. For example, quinapril originator price was 0.731 JD/DDD in 1997 and then it decreased to 0.630JD/DDD in 1999. Another decrease was observed in 2001 followed by a further decrease to 0.389 in 2003. Finally, quinalapril originator price reached 0.102 JD/DDD in 2010 (86% gradual decrease between 1997 and 2010) (Figure 3.31).

The price of fosinopril originator was 0.882 JD/DDD in 1995 and it showed gradual decrease in price throughout the period studied until it reached 0.493 JD/DDD in 2010 (a

percentage decrease of 44.1% since 1995). Another example is clizapril originator which decreased from 0.669 JD/DDD in 1995 to 0.415 JD/DDD in 2005 (Figure 3.31).

It is clear from figure 3.31, that the price of both originators and generics ACEIs was decreasing over time. The decrease in price of ACEIs could also be due to time in the market and originator/generic competition. In fact, the Pearson correlation test showed a statistically significant negative correlation ($P < 0.01$) between the number of ACEI originators, the number of ACEI generics and time with price of originator ($r = -0.856$, $r = -0.859$ and $r = -0.855$ respectively). It must be noted here that fosinopril generic was launched in 2007 at 0.393 JD/DDD, which is 28% cheaper form the price of originator at time of launch. Linispril generic price in 1995 was 26% cheaper than its originator (0.436 JD/DDD compared to 0.589JD/DDD for the originator). This illustrates how the prices of generics follow those of originators as per the pricing policy. In fact, the prices of ACEIs showed a significant positive correlation between the price of originators and generics ($r = 0.794$, $P < 0.05$).

Figure 3.31: Change of the prices of ACEIs (JD/DDD) over time



3.5 CONCLUSION

In summary, the results of this chapter were consistent with previous research held in the same area. Newly released innovative originators usually launch at higher prices than their predecessors which leads to an increase of the average prices of all available drugs within a class. This is because new drugs representing important therapeutic advance are usually priced at higher prices compared with their existing substitutes. However, imitative drugs are usually priced lower.[118]

The competition in the market is considered to be an important factor affecting the prices of medicines. The negative correlation between number of generics and mean prices of originators which is mainly seen in Jordan could be due to the competition between generics and originators within the class. However, in the UK this was not clearly seen by the correlation as the originators companies reduce their prices before the end of patency and before the generics entry, as was revealed in the cardiovascular price graphs studied.

The correlation between the time in the market and the prices of originators was found to significantly reduce the prices for many "me too" drugs in both countries. "Me too" drugs are priced cheaper as they do not have significant improvement than their predecessors. This strategy is used in order to promote market penetration and gain rapid acceptance. This was supported by previous research.[118]

New factors affecting the pricing of medicines were identified from this research. The change in treatment's protocols or guidelines was found to have an effect on medicines prices. Moreover, identifying new information (e.g. potential use, therapeutic evidence, etc.) about a marketed medicine was found to influence its price.

The market of pharmaceuticals in both countries was varied when it came to the pricing of medicines, with prices being influenced by different factors as identified above. Therefore, there is no single pricing factor that predicts the pricing behaviour of originator and generic medicines in Jordan or in the UK. However, competition, time and the pricing policy e.g. "price changes" allowance in PPRS in the UK, which allow for price increases based on increased value or decreases as appropriate, and the ceiling price on generics in Jordan can explain some of the trends observed.

CHAPTER FOUR

PRICE COMPARISONS

4.1 PRICE COMPARISONS

4.1.1 COST MINIMISATION ANALYSIS

Pharmacoeconomics as defined earlier in chapter 2 is "the description and analysis of the costs of drug therapy to health care systems and the society".[169] It identifies, measures, and compares the costs and consequences of pharmaceutical products and services.[68]

High medicine prices are of great concern to patients which can result in their non-compliance. Non-compliance can lead to reduced productivity and increased medical costs.[170] The prices of medicines have high economic implications on the public as well as on governments. A US nationwide survey of 1,010 adults in 2001 found that 22% chose not to fill prescriptions because of the price. This is equivalent to 20-30% overall rate of unfilled prescriptions.[171]

Pharmaceutical expenditure is a worldwide issue, with a greater impact on the developing countries. It is believed that medicine expenditure in developing and transitional countries accounts for around 20-60% of the health expenditure.[172] The majority of the population in low and middle-income countries have limited access to medications, mainly due to the lack of affordability or the poor availability of medicines.[172] In addition, it is reported that almost 90% of the public in developing countries pay for their medications through out-of-pocket payments.[173]

The CMA (section 2.3) is used to select the least costly therapy/intervention among multiple equivalent interventions. Examples include comparing brands with generics, which would achieve the same level of benefit at a reduced cost. [80-81] In CMA, the costs are identified, measured and compared in monetary units. The final analysis will show the "cost savings" of one treatment over another.[76] Comparing generic to originator brand in

each of the countries studied should allow highlighting the potential "cost saving" from generic utilisation.

4.1.2 INTERNATIONAL MEDICINE PRICES COMPARISON

A study was conducted in 1996 by Balasubramaniam [174] to compare the retail medicine prices in developing countries in the Asia Pacific Region with prices in selected developed countries. The study showed that the prices varied dramatically, with percentage differences varying from several hundred to several thousands, with extremely large ranges of differences for the developing countries.[174]

International price comparisons can provide powerful tools for advocacy and help to identify possible policy changes and lines of action to reduce high prices.[175] It helps policy makers to establish and tailor a proper pricing system to their unique socioeconomic nations' characteristics. It can also be used to evaluate the affordability of drugs in the domestic market.[176]

International price comparisons are challenging and the comparison of medicine prices between Jordan and the UK is no exception. International drug price comparisons are sensitive to measurement methods. Therefore, special care must be taken when making such comparisons.[177]

Normally, when making comparisons, the countries with which you compare your data should be similar in terms of economic wealth and development. However, as stated in chapter 1, in some cases, and depending on the purpose of the comparison, comparing very poor to very rich countries can carry powerful advocacy messages, e.g. to show that the prices in a relatively poor country are the same as in a relatively rich country.[14]

Ideally, when selecting drugs for international comparison they should be ones that have one major indication and are used in a similar manner across countries. Suitable drugs are those used for chronic diseases.[14] As package sizes, forms, strengths, indications, and ways of distributing drugs vary among countries, the comparison should be carried out using a standardised measure unit such as DDD [176] Moreover, the comparison should be carried out using a single currency unit.[178]

4.1.3 CAUSES OF PHARMACEUTICALS PRICE VARIATION ACROSS COUNTRIES

Price variation between countries could be due to several reasons. One of the main factors leading to price differences is the margin taken by wholesalers and retailers.[179] Another factor influencing price variation across countries is the differential pricing for pharmaceutical products.[146] According to a study which measured the cost of pharmaceuticals across Europe in 2011, prices of pharmaceuticals, particularly in-patent, seem to be proportionally higher in Member States with higher levels of income per capita.[179]

Governmental pricing policies play a major role in medicine price variation across countries. The price of medication in general is found to be significantly lower in countries that use price control regulations than countries that do not.[127]

Other factors that contribute to variation include; marketing strategy, therapeutic use of a drug, prescribing and dispensing habits, etc. as discussed in chapter 3.

4.2 AIM AND RATIONALE OF THIS CHAPTER

A previous study conducted by the researcher in 2008,[126] revealed that the prices of generics and originators of five drugs (omeprazole, lansoprazole, simvastatin, enalapril and lisinopril) in Jordan were higher than in the UK particularly for the generics. Generic drugs were found relatively expensive in Jordan and were 5–20 times more expensive than the equivalent prices of the same drugs in the UK. Therefore, this chapter aims to compare the prices of originator and generics between Jordan and the UK in order to provide conclusive evidence based on an extensive study. The expected savings by using generic medicines instead of originator medicines in both countries was also calculated. Moreover, a qualitative study seeking answers for the differences in prices between the two countries was conducted, by interviewing the key stakeholders.

4.3.1 A COMPARISON OF GENERIC AND ORIGINATOR BRAND DRUG PRICES BETWEEN JORDAN AND THE UK

4.3.1.1 DRUG SAMPLE SELECTION

The drugs used for this comparison were included according to the same inclusion/exclusion criteria as previously outlined in chapter 3.

Based on the inclusion criteria, 307 drugs were identified. The drug non-proprietary names were then matched for their availability in both countries. Only 178 drugs had matching originators available in both countries, whereas, only 50 drugs had matching generics in both countries.

4.3.1.2 DATA COLLECTION OF PRICES

The UK medicines prices used were based on those reported by the NHS in BNF 2010.[180] The Jordanian prices were obtained from the JFDA. The average price for available generics for each drug was used. These prices were converted into single currency unit (GBP) based on the average exchange rate in 2010 which was obtained from the Central Bank of Jordan (Appendix1).

Drug prices were expressed per DDD. The DDD was obtained from the WHO Collaborating Centre for Drug Statistics Methodology,[149] for each included drug. As explained in chapter 3 (section 3.2.2) the DDD was assumed to be 5ml for eye drops and for topical preparations (i.e. ointments/creams) the DDD was assumed to be 1 gram.

4.3.1.3 PRICING DATA ANALYSIS

Four types of price comparisons were conducted; percentage differences between the prices of generics in Jordan and in the UK, percentage differences between the prices of originators in Jordan and in the UK, percentage expected savings by substituting originators to generics in Jordan and percentage expected savings by substituting originators to generics in the UK. These comparisons were calculated and expressed in table format.

4.3.2 QUALITATIVE STUDY

To explore the underlying factors contributing to the prices of medicines in Jordan in comparison to the UK, qualitative interviews with key stakeholders were conducted. The interviews sought answers for the following questions: (1) how are medicine prices set in Jordan, (2) what factors may affect medicine prices, (3) how the introduction of a generic policy which encourages generic utilisation will affect medicines prices.

4.3.2.1 METHOD SELECTION

Research interviews are very commonly used in health care and pharmacy practice studies. They are a principal method in data collection for qualitative studies.[181] In-depth interviews are recommended for research dealing with highly sensitive subject matter.[182] Researchers can tap into personal experiences from participants about sensitive issues and gain clear explanations by using open questions and free probing. Interviews are often a flexible way of gathering information compared to a self-completion questionnaire. This study used 'the general interview guide approach', or in other words semi-structured interviews with an interview guide being prepared in the form of an index of topics to be discussed over the course of the study.[183] Because the index plays the role of a reminder, rather than a set of rigidly sequenced questions, the researcher was free to ask questions on whatever issue emerges while at the same time keeping the focus on a predetermined topic. The index only provided a framework for the interview. However, the actual direction of the discussed issues were determined by the respondent's experience, views, perceptions, etc.[181]

4.3.2.2 PARTICIPANTS RECRUITMENT

The logic of qualitative sampling is to gain a better understanding of the investigated issues.[184] Choosing study participants is based on their ability to provide the greatest chance of revealing data to answer the posed research questions.[185] Potential participants to be interviewed should be carefully selected, so random selection is not commonly recommended.[186] Purposive sampling was therefore used in this study. Purposive sampling is the primary approach used in qualitative research, as it targets appropriateness or selection of information-rich cases. Patton [183] defines purposive sampling as "those from which one can learn a great deal about issues of central importance to the purpose of the research".[183] Researchers should select good participants who are articulate, reflective, and willing to share experiences with the interviewer.[184]

In this study, four in-depth individual interviews were conducted. The first interview was with a representative of the pricing department at the JFDA, who represents the regulatory point of view. The local industry point of view was reflected by the Jordanian Association of Pharmaceutical Manufacturers (JAPM) representative and a business development manager form a local Jordanian manufacturer. Lastly, an interview with an owner of the main imported generics wholesaler in Jordan was conducted, to examine the imported medicines companies' point of view.

4.3.2.3 INTERVIEW INSTRUMENTS

A preliminary interview guide was constructed with nine broad topics for discussion to identify the root causes of medicine prices, opinions regarding the current pricing policy and affordability of medicines. The topics were as follows:

1. General opinion about the current pricing policy
2. Opinions about the use of Saudi Arabia as a reference country in the pricing policy
3. Factors taken into account when applying for pricing at JFDA
4. Reasons behind the high prices of medicines in Jordan compared to the UK
5. Export market or local Jordanian market
6. Bonuses effect on the prices of medicines
7. Marketing and promotion effect on the prices of medicines
8. Introduction of a generic utilisation policy
9. Categories for pharmacy profit

The full interview schedules are available in Appendices 4 and 5.

4.3.2.4 ETHICAL CONSIDERATION

This research followed the ethical research procedures of the ethics guidelines of the Research Ethics Committee of Kingston University, London (KU). Ethical clearance was obtained prior to conducting this research. This research did not deal with invasive information; consequently, ethical problems were not incurred.

Careful consideration was given to the ethical features of this study and the possible impact on participants who disclosed sensitive information. The confidentiality of the data including the identity of participants was maintained throughout the study.

A copy of the interview cover letter is included in Appendix 3 in English language. The cover letter detailed the purpose of the interview to be undertaken and assured the key informants/experts that the confidentiality will be maintained.

4.3.2.5 DATA COLLECTION AND ANALYSIS

4.3.2.5.a DATA COLLECTION

In-depth, semi-structured interviews were conducted from July 2012 to September 2012. Interviews took place wherever the participants chose, in their office, their home or a convenient place to assist with making them comfortable and at ease with this sensitive research.

Before each interview, the purpose of the study was briefly described and written informed consent obtained. Each in-depth interview lasted from one to two hours and was audio taped. One participant asked the researcher to stop audio taping when he talked about corruption. Another participant did not want to be taped at all. In these cases, the researcher was careful to respect the views of the study participant and responses were recorded by hand written notes instead. All interviews were conducted in Arabic.
Following the completion of each interview, *verbatim* transcription was undertaken (Appendix 6).

4.3.2.5.b INTERVIEW TRANSLATION

In order to achieve reliability and validity of the interviews used in this research, the interview were translated into the English language using a back-translated method. Precisely, interviews were conducted in Arabic and then were translated back to the English version. The pre-test version was sent to two Jordanian translators (Arabic/English people) to make sure that the two versions of the interviews matched as closely as possible. The English version was translated into Arabic by a professional Jordanian translator, and then translated back to English by another professional Jordanian translator working independently. The interviews for both language versions were discussed and compared to ensure that they were conceptually equivalent. The final drafts were then used for the main study.

4.3.2.5.c THEMATIC ANALYSIS

The most common analysis technique used in qualitative research is thematic analysis. [187] In order to describe the research phenomenon and answer the research question, patterns are usually identified through searching across the qualitative data.[188]

In order to conduct thematic analysis for this study, the participants' opinions were coded. These codes were then arranged according to the common similarities or relationship and combined in a way to reduce data to form conceptualized themes. Lastly, after an extensive comprehensive process of manual analysis of all transcripts and comparing the emerged themes back to the original transcripts, the data were grouped into major significant themes.[189-190]

The analysis was performed inductively where the themes emerged from the data 'rather than being imposed prior to data collection and analysis'.[183] To support the analysis and illustrate themes, exemplar were extracted and quoted in the results section.

4.3.2.5.d DATA PRESENTATION

Participants were numbered according to their interview order. Direct quotes from interviews are cited either within text, wherein quotes are cited as a separate paragraph presented in italics or between texts.

4.4 RESULTS

4.4.1 A COMPARISON OF GENERIC AND ORIGINATOR BRAND DRUG PRICES BETWEEN JORDAN AND THE UK

4.4.1.1 GENERIC DRUG PRICES COMPARISON

Table 4.1 shows the UK and Jordanian prices per DDD expressed in GBP for the 50 matching generic drugs in both countries used for chronic conditions. The drugs are listed in alphabetical order using the BNF therapeutics' system of classification.

Table 4.1: Generic medicines prices comparison between UK and Jordan.

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Gastro-intestinal system	H2 Receptor antagonists	cimetidine	0.534	0.301	-43.56%
		famotidine	0.158	0.356	125.48%
		ranitidine	0.048	0.317	560.82%
	Proton pump inhibitors	lansoprazole	0.107	0.769	618.72%
		omeprazole	0.063	0.691	997.06%
		pantoprazole	0.636	0.820	28.88%
Cardiovascular system	Antiarrhythmic	amiodarone	0.054	0.140	159.90%
	Beta blockers	atenolol	0.025	0.154	516.60%
		bisoprolol	0.211	0.215	1.95%
		carvedilol	0.163	0.410	151.25%
		metoprolol	0.143	0.520	263.62%
	Alpha blockers	doxazosin	0.058	0.511	781.03%
		terazosin	0.124	0.258	107.81%
	Angiotensin converting enzyme inhibitors	captopril	0.039	0.245	528.28%
		enalapril	0.041	0.176	329.29%
		fosonopril	0.126	0.359	184.86%
		lisinopril	0.038	0.221	481.24%
	Calcium channel blockers	amlodipine	0.04	0.322	705.27%
		nifedipine	0.2	0.274	36.90%
	Anti-platelet	dipyridamole	0.147	0.344	133.99%
	Statins	pravastatin	0.196	1.789	812.67%
		simvastatin	0.102	0.720	606.02%
	Fibrates	bezafibrate	0.265	0.245	-7.54%
		gemfibrozil	1.033	0.311	-69.93%
Respiratory system	Corticosteroids	beclometasone dipropionate (aerosol inhalation)	0.647	0.125	-80.66%
Central nervous system	Anti-psychotic drugs 2nd generations	amisulpride	0.849	1.297	52.75%
		risperidone	0.906	1.448	59.86%
	Tricyclic antidepressants	clomipramine	0.284	0.439	54.46%
	Selective serotonin reuptake inhibitors	citalopram	0.047	0.472	903.52%
		fluoxetine	0.038	0.375	886.90%
		paroxetine	0.086	0.520	504.62%
		sertraline	0.048	0.258	436.84%
	Other antidepressant	venlafaxine	0.157	0.985	527.21%
	Prophylaxis of migraine drugs	pizotifen	0.077	0.089	15.25%
	Control of epilepsies drugs	oxcarbazepine	1.333	0.800	-40.02%
		gabapentin	0.331	2.384	620.12%
		lamotrigine	0.289	2.101	626.85%
		sodium valproate	0.339	0.365	7.62%
	Dopaminergic drugs	bromocriptine	1.37	0.334	-75.60%

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Endocrine system	Sulphonylurea drugs	gliclazide	0.048	0.230	379.33%
		glimepride	0.068	0.132	94.55%
	Antithyroid	carbimazole	0.136	0.137	1.00%
	bisphosphonates and other drugs	alendronic	0.082	0.467	469.58%
Obstetrics, gynaecology, and urinary-tract disorders	Drugs used for urinary retention	doxazosin	0.354	1.957	452.77%
		terazosin	0.124	0.216	73.95%
Malignant disease and immunosuppressin	Gonadorelin analogues	flutamide	0.774	2.646	241.84%
	Non-steroidal anti-inflammatory drugs	meloxicam	0.104	0.312	199.76%
		nabumetone	0.219	0.434	98.03%
		tenoxicam	0.456	0.342	-24.95%
Eye	Beta blockers (eye)	timolol maleate	1.67	2.086	24.89%
Sources: UK prices BNF 2010, Jordanian Prices: JFDA 2010, Exchange Rate of 0.913 from Central Bank of Jordan 2010				Mean	290.42%
				Median	172.38%

As seen from Table 4.1 above, 43 of the 50 generic drugs (86%) were priced higher in Jordan compared to the UK. The median (mid-point) price difference was 172.38% higher in Jordan. The prices differences ranged from -80.66% to +997.06%. In general, Jordanian generic prices were on average around three fold higher than prices in the UK (+290.4%). However, the difference in prices for many drugs was significantly higher than the 3 fold difference. For example, the average price of pravastatin and amlodipine generics was more than eight fold higher than the UK price. Moreover, the average price of omeprazole, citalopram and fluoxetine generics were around 10 fold higher than the comparable UK price.

4.4.1.2 ORIGINATOR DRUG PRICES COMPARISON

Table 4.2 shows the UK and Jordanian prices per DDD expressed in GBP for the 178 matching originator brands in both countries, used for chronic conditions. The drugs are listed in alphabetical order by BNF therapeutics' system of classification.

Table 4.2 Originator prices comparison between UK and Jordan.

Originator brand medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Gastro-intestinal system	H_2 Receptor antagonists	cimetidine	0.754	0.685	-9.07%
		famotidine	0.907	1.166	28.61%
		nizatidine	0.527	0.794	50.84%
		ranitidine	0.043	0.311	625.01%
	Proton pump inhibitors	esomeprazole	0.991	1.584	59.85%
	Chelates and complexes	sucralfate	0.442	0.658	48.74%
		tripotassium phosphate	0.065	0.155	138.93%
	Prostaglandin analogues	misoprostol	0.067	1.275	1804.14%
	Proton pump inhibitors	lansoprazole	0.196	1.108	465.80%
		omeprazole	0.414	1.356	227.61%
		pantoprazole	0.735	1.069	45.56%
		rabeprazole	0.414	1.085	162.31%
	Aminosalicylate	olsalazine	0.706	0.915	29.70%
		sulfasalazine	0.249	0.445	78.79%
Cardiovascular system	Loop diuretics	bumetanide	0.054	0.082	53.38%
	potassium sparing diuretics	eplerenone	1.526	2.558	67.66%
	Anti arrhythmic	amiodarone	0.250	0.195	-21.77%
		flecainide	0.63	0.334	-46.86%
		propafenone	0.156	0.248	59.28%
	Beta blockers	atenolol	0.093	0.402	332.94%
		bisoprolol	0.453	0.217	-52.00%
		carvedilol	0.640	0.526	-17.77%
		metoprolol	0.138	0.417	202.60%
		nadalol	0.357	0.300	-15.90%
		nebivolol	0.330	0.387	17.48%
		pindolol	0.314	0.285	-9.14%
	Alpha blockers	doxazosin	1.006	0.827	-17.79%
		terazosin	0.153	0.320	109.78%
	Angiotensin converting enzyme inhibitors	captopril	0.327	0.322	-1.50%
		clizapril	0.262	0.378	44.46%
		enalapril	0.376	0.340	-9.44%
		fosonopril	0.576	0.449	-21.91%
		imidapril	0.263	0.438	66.65%
		lisinopril	0.073	0.424	481.49%
		moexipril	0.249	0.370	48.76%
		perindopril	0.303	0.356	17.70%
		quinapril	0.921	0.093	-89.88%
		ramipril	0.258	0.304	18.16%
		trandolapril	0.235	0.354	50.77%
	Angiotensin II receptor antagonists	candesartan	0.353	0.534	51.54%
		telmisartan	0.446	0.615	37.99%
		eprosartan	0.511	0.700	37.10%
		irbesartan	0.457	0.686	50.28%
		losartan	0.457	0.695	52.29%
		valsartan	0.499	0.748	50.08%

Originator brand medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Cardiovascular system	Renin inhibitors	aliskiren	0.707	1.067	51.00%
	vasodilators	naftidrofuryl	0.59	0.533	-9.53%
	Centrally acting antihypertensive	moxonidine	0.410	0.348	-14.98%
	Other anti angina	ivabradine	1.393	2.059	47.82%
	Calcium channel blockers	amlodipine	0.396	0.483	22.01%
		felodipine	0.154	0.288	87.50%
		isradipine	0.591	0.681	15.23%
		nifedipine	0.248	0.354	42.87%
		nimodipine	3.733	0.376	-89.92%
	Antiplatelets	clopidogrel	1.212	1.815	49.78%
	Anticoagulants and protamine	acenocoumarol	0.214	0.117	-45.17%
		dabigatran	4.200	4.929	17.37%
		rivaroxaban	4.500	6.085	35.23%
	Bile acid sequestrants	cholestramine	1.152	0.874	-24.11%
	Antifibrinolytic	tranexamic acid	0.238	0.522	119.44%
	Statins	atorvastatin	0.880	1.311	49.03%
		fluvastatin	1.635	1.527	-6.56%
		pravastatin	1.549	2.236	44.37%
		rosuvastatin	0.644	0.831	29.15%
		simvastatin	1.932	0.816	-57.72%
	Ezetmibe	ezetimibe	0.940	1.221	29.97%
	Fibrates	bezafibrate	0.264	0.431	63.41%
		fenofibrate	0.518	0.280	-45.81%
		gemfibrozil	1.270	0.422	-66.76%
Respiratory system	Adrenoceptor agonists	formetrol fumarate (foradil)	1.002	0.806	-19.48%
		formetrol fumarate (oxis turbohaler)	0.827	0.606	-26.62%
		salmetrol (accuhaler)	0.975	0.663	-31.97%
		salmetrol (diskhaler)	1.193	0.463	-61.17%
		salmetrol (evohaler)	0.975	0.561	-42.42%
	Antimuscarinic bronchodilators	ipratropium bromide (aerosol inhalation)	0.152	0.228	50.31%
	Antimuscarinic bronchodilators	tiotropium (inhalation powder)	1.209	1.355	12.12%
		tiotropium (solution for inhalation)	1.209	1.771	46.53%
	Corticosteroids	budesonide (dry powder for inhalation)	0.74	0.531	-28.24%
		mometasone furoate(twisthaler dry powder inhaler)	0.726	0.862	18.79%

Originator brand medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Respiratory system	Cromoglicate & related therapy	sodium cromoglicate (sodium cromoglycate) aerosol inhalation	1.060	1.219	15.04%
	Leukotriene receptor antagonists	montelukast	0.963	1.854	92.58%
		zafirlukast	0.634	1.018	60.58%
Central nervous system	Antipsychotic drugs	flupentixol	0.195	0.394	102.47%
		trifluoperizine	0.175	0.177	1.50%
		zuclopenth	0.169	0.314	86.24%
	Antipsychotic drugs 2nd gen	amisulpride	1.180	1.621	37.39%
		aripiprazole	3.488	3.883	11.33%
		olanzapine	2.838	4.336	52.82%
		quetiapine	3.770	0.135	-96.40%
		risperidone	2.670	1.739	-34.86%
	Antimanic drugs	valproic acid	0.810	0.510	-36.94%
	Tricyclic & related antidepressant	clomipramine	0.288	0.550	91.20%
		nortriptyline	0.721	0.121	-83.15%
	Selective serotonin reuptake	citalopram	0.533	0.813	52.62%
		escitalopram	0.533	0.875	64.33%
		fluoxetine	0.167	0.464	178.23%
		fluvoxamine	0.570	0.503	-11.74%
		paroxetine	0.423	0.589	39.42%
		sertraline	0.636	0.289	-54.42%
	Other antidepressant drugs	duloxetine	0.990	1.543	55.91%
		flupentixol	0.340	0.394	16.12%
		reboxetine	0.472	0.522	10.72%
	CNS stimulants & attention deficit hyperactivity disorder drugs	atomoxetine	2.974	5.154	73.32%
	Drug used for obesity	orlistat	1.152	2.535	120.12%
		sibutramine	0.893	0.703	-21.19%
	Prophylaxis migraine	pizotifen	0.153	0.310	103.01%
	Control of epilepsies	gabapentin	2.544	3.017	18.62%
		lamotrigine	3.082	2.416	-21.58%
		levetiracetam	2.615	4.082	56.13%
		oxcarbazepine	1.340	0.883	-34.04%
		pregabline	1.150	1.827	58.91%
		topiramate	2.895	4.209	45.42%
		vigabatrin	1.234	1.674	35.70%
	Dopaminergic drugs	amantadine	0.579	0.237	-58.91%
		bromocriptine	0.267	0.748	180.34%
		entacapone	2.917	5.364	83.91%
		paramipexole	9.095	6.976	-23.29%

Originator brand medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Central nervous system	Antimuscarinic	procyclidine	0.236	0.179	-23.96%
	drugs for dementia	donepezil	3.404	3.481	2.29%
		galantamin	2.440	2.633	7.92%
		memantine	2.465	2.608	5.80%
		rivastigmine	1.781	2.524	41.73%
	Drugs used in essential tremor	pirecetam	0.366	0.590	61.24%
Endocrine system	Sulphonylurea	glimepride	0.238	0.239	0.70%
	Other antidiabetic drugs	acarbose	0.386	0.490	26.96%
		pioglitazone	1.188	0.913	-23.15%
		repagline	0.261	0.431	65.43%
		rosiglitazone	1.071	1.286	20.14%
		ritagliptin	1.188	0.959	-19.25%
		vildagliptin	1.134	1.018	-10.15%
	Antithyroid	carbimazole	0.116	0.124	7.40%
	Calcitonin	calcitonin	1.500	2.640	76.06%
	Bisphosphonates & other drugs	alendronic	0.826	1.024	24.00%
		ibrandronic	0.613	1.184	93.29%
		risedronate	0.656	0.878	33.96%
		strontium ranelate	0.914	1.419	55.30%
	Bromocriptine & other drugs	quinagolide	0.900	0.871	-3.11%
Obstetrics, gynaecology, and urinary-tract disorders	Drugs for urinary retention	alfuzosin	1.019	0.648	-36.38%
		doxazosin	3.771	3.065	-18.70%
		terazosin	0.153	0.321	109.99%
	Drugs for urinary frequency	duloxetine	1.980	1.543	-22.05%
		flavoxate	0.519	0.687	32.40%
		oxybutynin	0.458	0.219	-52.03%
		solifenacin	0.921	1.130	22.70%
		tolterodine	1.091	1.139	4.46%
Malignant disease and immunosuppression	Antiproliferative immune	mycophenolate	0.839	2.985	255.83%
	progestogens	medroxyprogesterone	4.89	0.613	-87.45%
		megestrol	0.664	1.739	162.01%
	hormone antagonists	anastrozole	2.450	3.699	50.99%
		exemestane	2.960	4.006	35.34%
		letrozole	2.375	5.108	115.11%
	Gonadorelin analogues	bicalutamide	4.571	5.934	29.83%
		cyproterone	0.889	1.202	35.22%
Nutrition and blood	Iron overload	defrasirox	8.400	12.055	43.52%
		defriprone	1.524	1.409	-7.53%

Originator brand medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	UK	Jordan	
Musculoskeletal and joint diseases	Non-steroidal anti-inflammatory	aceclofenac	0.315	0.352	11.75%
		celecoxib	0.718	0.689	-4.03%
		etoricoxib	0.718	1.092	52.21%
		meloxicam	0.431	1.212	181.32%
	Long term control of gout	sulfasalazine	0.075	0.089	18.87%
	Drugs that enhance neuromuscular transmission	pyridostigmine	0.722	0.380	-47.32%
	Skeletal muscle relaxants	baclofen	0.129	0.207	60.87%
		tizandine	0.667	0.227	-65.97%
Eye	Beta blockers (eye)	betaxolol	1.940	4.152	114.07%
		carteolol	4.600	9.222	100.48%
		levobunolol	1.850	4.670	152.46%
		timolol maleate	3.120	3.842	23.15%
	Prostaglandin analogues (eye)	bimatoprost	17.17	22.835	33.02%
		latanoprost	24.96	27.471	10.06%
		travoprost	20.34	27.471	35.06%
	Carbonic anhydrase inhibitors	acetazolamide	0.340	0.455	33.99%
		brinzolamide	6.690	8.593	28.45%
		dorzolamide	6.330	10.537	66.47%
	Sympathomimetics (eye)	brimonidine	6.850	8.512	24.27%
Skin	Preparation for psoriasis	calcipotriol	0.193	0.349	81.47%
		calcitriol (1,25-dihydroxycholecalciferol)	0.139	0.379	173.70%
	Drug affecting immune response	pimecrolimus	0.656	1.057	61.19%
		tacrolimus	0.648	1.090	68.24%
Sources: UK prices BNF 2010, Jordanian prices: JFDA 2010, exchange rate of 0.913 from central bank of Jordan 2010				Mean	51.47%
				Median	33.49%

According to Table 4.2, 126 out of the 178 originators (70.79%) were priced higher in Jordan compared to the UK. The median (mid-point) price difference was 33.49% higher in Jordan. The prices differences ranged from -96.40% to +1804.14%. In general, Jordanian originator prices were on average more than 1.5 fold higher than the prices in the UK (+51.47%). However, many originators were extremely higher than this average. For example, the Jordanian price of misoprostol originator tablets was around 19 times the comparable UK price. The price of ranitidine originator in Jordan was more than seven times the UK price, and lansoprasole originator was around 6 times more than the price in the UK.

4.4.1.3 AVERAGE EXPECTED SAVING BY GENERIC SUBSTITUTION IN JORDAN

Table 4.3 shows the average Jordanian prices per DDD expressed in GBP for the originator drugs included that had matching generic drugs. The table shows the % difference in price between each originator drug and the average price of all the bioequivalent generics available. Drugs are listed in alphabetical order using the BNF therapeutics' system of classification.

Table 4.3: Differences between originator and generic prices in Jordan

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active Ingredient	Originator brand	Average Generics	
Gastro-intestinal system	H_2 Receptor antagonists	cimetidine	0.685	0.301	-56.04%
		famotidine	1.166	0.356	-69.46%
		ranitidine	0.311	0.317	1.75%
	Proton pump inhibitors	lansoprazole	1.108	0.769	-30.65%
		omeprazole	1.356	0.691	-49.04%
		pantoprazole	1.069	0.819	-23.39%
Cardiovascular system	Anti arrhythmic	amiodarone	0.195	0.140	-28..24%
	Beta blockers	atenolol	0.402	0.154	-61.71%
		bisoprolol	0.217	0.215	-1.06%
	Alpha blockers	doxazosin	0.827	0.444	-46.31%
	Angiotensin converting enzyme inhibitors	captopril	0.322	0.245	-23.93%
		enalapril	0.340	0.176	-48.31%
		fosonopril	0.449	0.358	-20.20%
		lisinopril	0.424	0.220	-47.97%
	Calcium channel blockers	amlodipine	0.483	0.322	-33.33%
	Statins	simvastatin	0.816	0.720	-11.83%
	Fibrates	bezafibrate	0.431	0.245	-43.20%
		gemfibrozil	0.422	0.310	-26.43%
Central nervous system	Antipsychotic drugs 2nd generation	amisulpride	1.621	1.296	-20.01%
		risperidone	1.739	1.448	-16.72%
	Tricyclic antidepressants	clomipramine	0.550	0.438	-20.33%
	Selective serotonin reuptakes	citalopram	0.813	0.471	-42.02%
		fluoxetine	0.464	0.375	-19.29%
		paroxetine	0.589	0.519	-11.83%
		sertraline	0.289	0.257	-11.11%
	Prophylaxis of migraine	pizotifen	0.310	0.088	-71.43%

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active Ingredient	Originator brand	Average Generics	
Central nervous system	Control of epilepsies	oxcarbazepine	0.883	0.799	-9.54%
		gabapentin	3.017	2.383	-21.01%
		lamotrigine	2.416	2.100	-13.09%
	Dopaminergic drugs	bromocriptine	0.748	0.334	-55.34%
Endocrine system	Sulphonylurea	glimepride	0.239	0.1322	-44.80%
	Antithyroid	carbimazole	0.124	0.137	10.25%
	Bisphosphonates and other drugs	alendronic acid	1.024	0.467	-54.40%
Obstetrics, gynaecology, and urinary-tract disorders	Drugs used for urinary retention	doxazosin	3.065	1.956	-36.17%
		terazosin	0.321	0.215	-32.86%
Musculoskeletal	Non-steroidal anti-inflammatory drugs	meloxicam	1.212	0.3117	-74.29%
Eye	Beta blockers	timolol maleate	3.842	2.085	-45.72%
Source: Jordanian prices: JFDA 2010, exchange rate of 0.913 from central bank of Jordan 2010				Average	-32.68%
				Median	-30.65%

From Table 4.3, it can clearly be seen that the majority of generic drugs studied (73%, n= 35) were priced less than their equivalent originator in 2010. The range of price difference between originators and generics was from +10.25% to -74.29% with an average price difference of -32.68%. The median (mid-point) price difference was -30.65%. Surprisingly, for two drugs, carbimazole and ranitidine, the difference between the originator and average generic price was +10.25% and +1.75% respectively. Also for 22% of the drug sample studied (8 out of 37), the generic substitution saving was less than 20%, which is the minimum saving expected according to the generic pricing policy in Jordan which caps the price of a generic at 80% of the price of the originator, this could be due the fact that the 80% applies at the time of registration and re-registration (after five years) of the generic product. Originators might drop their price; however this may not be reflected in generic prices. This suggests that a more frequent pricing review should be adopted by the JFDA.

4.4.1.4 AVERAGE EXPECTED SAVING BY GENERIC SUBSTITUTION IN UK

Table 4.4 shows the average UK prices per DDD expressed in GBP for the originator drugs included that had matching generic drugs. The table shows the % difference in price between each originator drug and the average price of all the bioequivalent generics available. Drugs are listed in alphabetical order using the BNF therapeutics' system of classification.

Table 4.4: Differences between originator and generic prices in UK

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	Originator brand	Average generics	
Gastro-intestinal system	H_2 Receptor antagonists	cimetidine	0.754	0.534	-29.18%
		famotidine	0.907	0.158	-82.58%
		ranitidine	0.043	0.048	11.63%
	Proton pump inhibitors	lansoprazole	0.196	0.107	-45.41%
		omeprazole	0.414	0.063	-84.78%
		pantoprazole	0.735	0.636	-13.47%
Cardiovascular system	Anti arrhythmic	amiodarone	0.250	0.054	-78.40%
	Beta blockers	atenolol	0.093	0.025	-73.12%
		bisoprolol	0.453	0.211	-53.42%
		carvedilol	0.640	0.163	-74.53%
		metoprolol	0.138	0.143	3.62%
	Alpha blockers	doxazosin	1.006	0.058	-94.23%
		terazosin	0.153	0.124	-18.95%
	Angiotensin converting enzyme inhibitors	captopril	0.327	0.039	-88.07%
		enalapril	0.376	0.041	-89.10%
		fosonopril	0.576	0.126	-78.13%
		lisinopril	0.073	0.038	-47.95%
	Calcium channel blockers	amlodipine	0.396	0.040	-89.90%
		nifidipine	0.248	0.200	-19.35%
	Statins	simvastatin	1.932	0.102	-94.72%
	Fibrates	bezafibrate	0.264	0.265	0.38%
		gemfibrozil	1.270	1.033	-18.66%
Central nervous system	Antipsychotic drugs 2nd gen	amisulpride	1.180	0.849	-28.05%
		risperidone	2.670	0.906	-66.07%
	Tricyclic antidepressnt	clomipramine	0.288	0.284	-1.39%
	Selective serotonin reuptake	citalopram	0.533	0.047	-91.18%
		fluoxetine	0.167	0.038	-77.25%
		paroxetine	0.423	0.086	-79.67%
		sertraline	0.636	0.048	-92.45%
	Prophylaxis migraine	pizotifen	0.153	0.077	-49.67%

Generic medicines			Prices (GBP/DDD)		% price difference
System	Class	Active ingredient	Originator brand	Average generics	
Central nervous system	Control of epilepsies	oxcarbazepine	1.34	1.333	-0.52%
		gabapentin	2.544	0.331	-86.99%
		lamotrigine	3.082	0.289	-90.62%
	Dopaminergic drugs	bromocriptine	0.267	1.370	413.11%
Endocrine system	Sulphonylurea	glimepride	0.238	0.068	-71.43%
	Antithyroid	carbimazole	0.116	0.136	17.24%
	Bisphosphonates and other drugs	Alendronic acid	0.826	0.082	-90.07%
Obstetrics, gynaecology, and urinary-tract disorders	Drugs for urinary retention	doxazosin	3.771	0.354	-90.61%
		terazosin	0.153	0.124	-18.95%
Muscloskeletal	Non-steroidal anti-inflammatory drugs	meloxicam	0.431	0.104	-75.87%
Eye	Beta blockers	timolol maleate	3.120	1.670	-46.47%
Source: UK prices BNF 2010				Average	-43.54%
				Median	-71.43%

From Table 4.4, it is clear that the majority of generic drugs studied (83%, n= 34) were priced lower than their originators in 2010. The range of price difference between originators and generics was from +413.11% to -94.72% with an average price difference of -43.54%. The median (mid-point) price difference was -71.43%. It must be noted that for more than half of the sample (51%) the average saving exceeded 84% and more than 30% of the sample studied achieved more than 90% saving.

For 5 of the drugs studied, the originator prices were higher than the generics. Two of these medications namely; ranitidine and carbimazole showed the same trend in Jordan.

When excluding one outlier i.e. the drug for which the difference in price was more than +20% (bromocriptine); the median price difference became -72.27% with an average saving of 54.96%. According to the trends observed in chapter 3, many marketing authorisation holders in the UK, opt to lower their originators prices significantly at the end of the patent, to protect their market share from competition with generics which could explain the positive differences in the prices quoted above.

4.4.2 QUALITATIVE INTERVIEWS RESULTS

From the four interviews conducted, 15 main themes and 6 sub-themes were identified. One of the main themes was that the pricing policy satisfies both local manufacturers and originator companies whereas it doesn't satisfy imported generics wholesalers as the imported generics prices are based on the country of origin or ex-factory prices plus a profit basis.

The interviews also found that the stakeholders involved were not supportive of the policies that increase generic utilisation such as generic prescribing and generic substitution. The suggestion to register the local generic drug in two different names; one with a low price to support the local market and the other with a higher price to support the local industry to achieve high profits in the exportation markets was not favoured.

The analysis also revealed a number of factors contributing to the high medicines prices within the following themes; the pricing policy is the main reason for the high price of originators and generics in Jordan compared with the UK, there is a problem in the application of the policy, low demand in the small Jordanian market is the reason why local manufacturers request the highest price possible. Other themes identified included the following; the competition in the market is between generics and originators and not generics themselves, the industry in Jordan is private and profit seeking, the local generic industry and the originator multinational companies wholesalers are influencing the pricing policy.

Other themes that emerged from this study were; reference pricing determines the prices of pharmaceuticals worldwide, promotion and marketing expenses do not contribute to the price of products in Jordan, the bonus in Jordan is viewed as a marketing tool, selling through tenders at low prices is another route of marketing and achieves high profit and that some medicines are priced at the 80% of originator price although they are imported and just packaged by local manufacturers.

The above themes and many others are discussed in detail below.

Theme 1: Pricing policy only satisfies originators' wholesalers and local generic manufacturers

The current Jordanian pharmaceuticals pricing policy satisfies the local generic manufacturers and multinational originator companies. According to the interviewees, the policy is good, balanced and meets expectations by allowing for high net profits. However, the policy does not satisfy imported generic wholesalers.

"it is good and balanced despite some flaws." **R2**

*"As Jordanian pharmaceutical company, these prices are up to our aspirations."***R3**

*"The net profit is usually very high."***R3**

"The rules preferred to serve foreign manufacturers of the originator (multinational companies) and Jordanian local generic industry companies." **R4**

"The rules care for the respective interests of originators and generics made locally only. However, they fail to consider imported generics such as those coming from Korea, China and India etc" **R4**

Theme 2: Local generic pricing allows for high profit margin

The current policy allows for local generic manufacturers to price their product up to 80% from the originator price. Almost all local generic manufacturers price their product at 80% of originator price but not less, which achieves high profits in both local and export markets, taking into account the low production costs. However, there are no incentives for local generic manufacturers to reduce their local prices in Jordan.

"The profit made by local companies is very high compared to the very low costs. The 80% rate serves Jordanian factories a lot because the productive cost is very low. I largely depend on the foreign market for exportation especially the Arab market, which requires to know about the price in the country of origin. Jordanian laws are serving me, so why should I not benefit from them?" **R3**

"The profit made by local companies is very high compared to the very low costs. The 80% rate serves Jordanian factories a lot because the production cost is very low." **R3**

"The cost of the medicine depends on the cost of raw material in China or India. Basically, the production cost is very low and other costs only relate to marketing." **R3**

"But why should I not get the highest profit possible in respect of the Jordanian market? " **R3**

"This is a high rate and is illogical. It does not deserve to be more than 50% of originator price" **R4** *"This also means that the 80% is too much exaggerated."* **R4**

Theme 3: Local generic industry and originator wholesalers influencing the policy

In Jordan, the local generic industry and originator wholesalers are influencing policy and have a big say in it. According to the regulatory body representative, they faced pressures from local generic manufacturers when they suggested making the maximum price for local generics 70% of the originator price. Pressure was also exerted on them when they changed the reference pricing basket to use 16 rather than 7 countries. However, the companies accepted the median of no less than 4 countries to determine the price. The original suggestion of using the average of the lowest 4 countries as reference price was strongly opposed. The local manufacturers' representative said that they exerted pressure because the export market base their prices on the country of origin price, hence the local price will affect the price at the exportation market which is the main profit generating market for them.

*"The preliminary suggestion was to recommend the use of the average of the lowest four states. However, pressures were exerted on the pricing committee by the originator and generic companies, the latter of which define their prices based on the originator's."***R1**

*"We would not do that otherwise the Jordanian manufacturers will rise and say "Support me and support my industry and I will in turn export products."***R1**

"It was 70% in the proposed rules but was changed into 80% under the pressures of factories and the Jordanian association of Pharmaceuticals Manufacturers Producers so the rate returned to 80%." **R1**

"Pressure is exerted on us by local producers. Even on the originators there is a pressure. When we changed the Median to take 16 instead of 7, they put on lots of

pressures until I had to take the median on no less than 4 states. It is because they are the ones to benefit." **R1**

"when exporting the medicine, there will be negotiations to reduce the price less and less. This is why all are requiring the ceiling to be 80%." **R2**

Theme 4: The policy is the main reason for the high price of originators and generics in Jordan compared with the UK

The high prices of originator compared with the UK, are mainly due to the pricing policy and the application of it. According to the regulatory body personnel, the reference countries used for the pricing of originators are the ones with a high income. The high prices of originators benefit the local manufacturers as the policy allows them to price the generics at 80% of originator price.

*"The rules give a high price for the originators "***R1**

*"As I told you it is the rules. However, we look at the prices of the originators in the UK and we do not find a significant difference. But it turns out that we are taking prices as if we were in Europe. My reference is Saudi Arabia and Europe. We are talking here about high-income countries while Jordan is a low-income country."***R1**

*"Jordanian companies are benefiting from the price of the originators and the principle of pricing that bound us to charge up to 80% of the originator's price. Differences in pricing policies between Jordan and Britain are the biggest and main factor for that".***R3**

The high prices of local generics in Jordan compared to the UK are also due to the pricing policy as it cut competition, as all generics' manufacturers price their products at the 80% ceiling price. However, this percentage margin does not reflect the pricing in neighboring countries with a similar demographic.

*"Here in Jordan there is no competition. Everyone is happy with the high price and is reluctant to reduce it. So it becomes like an implicit agreement as if they were saying to each other: this is my 80% so please do not reduce our price to less than this one. This means there is no competition."***R1**

"Most generics in Jordan are locally made. The pricing rules state that the local industry takes 80% of the originator's price. The price of the originator must be controlled from the very beginning. The question is why does the Jordanian industry takes 80%, generics in Egypt takes 60-65% from originator price, generics in Turkey takes 50-60% and in Saudi Arabia, the price of generic is gradually decreasing from 70% for the first time until 50%. There is a mistake in the pricing rules, which provide 80% of the originator's price for locally produced generic. This is a high rate and is illogical. It does not deserve to be more than 50% of originator price" **R4**

Theme 5: Reference pricing determines the prices of pharmaceuticals worldwide

In general, the country of origin's price decides the price of imported medicines all over the world.

*"This is the policy in all countries in the world. Reference is made always to the country of origin. For example, Jordan makes a condition for every medicine that its price in the country of origin is higher than that here. The Jordanian medicine follows the same rule."***R1**

"The nature of pricing in the Arab world is to consider the price to the public of the country of origin as the selling price for other markets." **R2**

"Importing countries require knowing the price of the country of origin. The targeted market is the foreign market." **R3**

"I largely depend on the foreign market for exportation especially the Arab market, which requires knowing about the price in the country of origin." **R3**

Theme 6: Export rather than the local market determines the prices of medicines

The main factor why local generic manufacturers request the highest possible price is that they depend on exportation markets. High local prices provide them with a high country of origin price to start negotiations to reasonable prices. The local market is small in size, so manufacturers do not rely on this market to recoup expenses and make a profit.

"80% of the originator's price in a small market like Jordan achieves for me less profit that those achieved by 50% rate in a gigantic supply-demand market." **R2**

"The Jordanian market is not a significant one neither is it targeted by originators' companies or the Jordanian generic companies. The Jordanian market is very small compared with international markets. This is why the price here is much higher." **R3**

"All international companies claim that Jordan's market is very small" **R4**

"I need to see the target market and the markets available to me and how much it is priced here and there in addition to expectations on sale volume." **R2**

"for exportation it takes 80% because all states require the price of the country of origin first then it is negotiated." **R2**

"when exporting the medicine, there will be negotiations to reduce the price less and less. This is why all are requiring the ceiling to be 80%." **R2**

"I largely depend on the foreign market for exportation especially the Arab market, which requires knowing about the price in the country of origin. Jordanian laws are serving me, so why should I not benefit from them?" **R3**

Theme 7: Referencing the prices with Saudi Arabia can be negative or positive

When the participants were asked about Saudi Arabia as a pricing reference, there were mixed views.

"It is an indicator that benefits Jordan in some cases." **R2**

"The Saudi society is very large and has a per capita income close to that of Jordan. Yes, there are extremely rich Saudis, but the majority's per capita income is similar to that of Jordanians if not less in some cases. Incomes are similar and so are the prices. I noticed that in the IMS pricing data. This is unlike other markets that show high prices of medicine." **R3**

"Saudi Arabia uses more than 33 countries in pricing while Jordan relies only on 16; I wish that the same pricing rules are used in Jordan" **R4**

Some participants think, if Jordan pricing policy was fully connected and referenced to Saudi Arabia policy this will ultimately reduce generic prices. According to one interviewee, Saudi Arabia prices the first generic at 70% of the originator price, with this

percentage decreasing as the number of generics increase. However, the correct percentage is 65% of the originator price decreasing as per 2010 Saudi pricing policy.[191]

"If the pricing of Jordan is linked to exportation to Saudi Arabia automatically, the price will be reduced in Jordan accordingly. This is because the price in Saudi Arabia for the generic is priced in a decreasing manner: from 70% to 60% then 50% of the originator's price." **R2**

*"We note that prices in Saudi Arabia are 25% lower than in Jordan. If same rules are applied in Jordan, prices are to be less by 25% in Jordan."***R4**

On the other hand, two interviewees believed that fully referencing Jordan medicines' prices with Saudi Arabia will increase the prices of originators and old medicines.

"the older medicines are much cheaper than in Saudi Arabia and it is we that started before Saudi Arabia. Saudi Arabia later adopted a very good plan in respect of the generics, i.e 70% then lower and lower." **R1**

"In light of my knowledge of both Saudi and Jordanian markets, prices in Saudi Arabia can be higher than in Jordan and vice versa." **R3**

Theme 8: Price competition between generics and originators and not generics

The current pricing policy, trigger more competition between generics and originators versus generics themselves, as by law, the prices of generics do not exceed 80% of the originator prices, so 20% is saved by using generic medicines. However, all local generic manufacturers price generics at the same level with minor differences of 3-5% only, hence minimising the price competition between generics.

*"Here in Jordan there is no competition. Everyone is happy with the high price and is reluctant to reduce it. So it becomes like an implicit agreement as if they were saying to each other: this is my 80% so please do not reduce our price to less than this one. This means there is no competition."***R1**

"There is competition but in quality. Most prices of the generic medicines are almost the same (with a slight difference margin of 3-5%). The price is an important factor in competing with the generic medicine but its role will be clearer when competing with the originators." ***R3***

"To get the highest price as long as this is legal while keeping at the same time for myself a margin of-20% to compete with the originator". **R3**

Theme 9: Production and marketing costs do not impact prices

Production and marketing costs are not accounted for when calculating the price of a drug, but they affect the overall profit margin of a company. The prices in Jordan are decided by the ceiling of 80% of the originator price.

"They are not related to the price of the medicine but to the profit making. The price of the medicine cannot be higher than the 80% rate." **R2**

"As for their impact, they do not have any impact. The price is defined on the basis of the 80% rule." **R4**

One interviewer suggested that a product can monopolise the market not through a marketing strategy, but through incentives provided to prescribers and pharmacists to increase the market share.

"I am not with exaggerated marketing especially because it incurs additional costs on the companies, which consider them when calculating profit before offering the medicine. This cost is by the way not added to the price because as I know the ceiling is 80%. Some products are monopolised by some companies not because of high costs of production or difficulties but because some companies have better competitive edge and afford distinguish gifts to be given to pharmacists and doctors." **R3**

As a result of the comment regarding gift incentives to monopolise the market share, the interviewees were asked if there is a code of conduct to govern this. The regulator stated yes and the imported generics wholesaler agreed but did not think it was always followed.

"there is a code of ethics followed by the companies" **R1**

"There is a code of ethics in Jordan but is not observed." **R4**

Theme 10: Bonus viewed as a marketing tool

The local generic companies view bonuses as a marketing tool that helps pharmacy to make big profits. The bonus is seen as a tool for competition which reflects that the prices of local generic medicines are very high and too much exaggerated and need to be controlled (please refer to section 2.8.6 for the definition of a bonus system).

"100% marketing Tools." **R2**

"Bonus is a marketing tool[....] A pharmacist can also through the selling of the generic medicine make lots of profit particularly with the high bonus, so he can sell a medicine and have its total price as a profit if he obtained that medicine through the bonus system." **R3**

"This means that they are using the bonus rather than the price itself for competition." **R1**

*"In Saudi Arabia, it was abandoned, we did the same for some period of time but will consider it, it needs to be controlled"***R1**

"This is a mistake. There are more than 21 local producers who make the same product. They are in competition. If I had the authority to define the manufactured products, I would have eliminated the bonus. This also means that the 80% is too much exaggerated." **R4**

The interviewees proposed a solution for the bonus issue. One suggestion was for an improved pricing policy with low prices. The other one was adopted from the experience of western countries e.g. the UK, in which a comprehensive medical insurance is set up where pharmacists are contracted to offer services. The last solution, proposed by the imported generic wholesalers' representative, was to introduce pharmacists' dispensing fees to facilitate the elimination of bonuses.

"What we need is a pricing policy that sets low prices or alternatively a comprehensive medical insurance plan should be put in place so that all pharmacies are contracted with and companies will compete in the same manner as in the western countries." **R1**

"To sort out this problem, there is a need to impose technical fees on the disbursement of a medicine as in the case of a doctor who charges for diagnosis at fixed prices. In relation to the above example, the profit gained through the bonus can be compensated for by the technical fees of the pharmacist for each prescription." **R4**

Theme 11: Introducing categories for pharmacy profits

The suggestion of introducing categories for pharmacy profits mark-up according to the cost of drugs was welcomed by the stakeholders involved. This is applicable in other countries such as Saudi Arabia. This could provide saving to the patients as the current fixed profit margin may make pharmacists eager to sell expensive medicines, which has a negative impact on patients in Jordan.

"We are now considering the fact that profit rates change and become in categories. Expensive drugs have lower profits and those with little profit will have higher profit margins." **R1**

"It should not be the case that for a JD100 medicine the pharmacist gets JD26. It is a high rate. There must be segments of profits depending on the price of medicine that must be decreasing when the price gets higher." **R2**

*"The fixed rate serves pharmacists a lot. This makes them eager more to sell expensive medicine, but this does not serve the people. This is the opposite to what happens in other countries like Saudi Arabia, which provides for categories of profits made by selling medicine. 50 up to 100 Rials has a high rate while 100 to 200 has a lower rate. This serves the patient"***R3**

"The fixed rate serves pharmacists a lot. This makes them eager more to sell expensive medicine, but this does not serve the people." **R3**

Theme 12: Selling through tenders is another marketing strategy

According to participants, selling through tenders is another route of marketing for local generic manufacturers. Selling through tenders achieves high net profit even at very low prices.

"The government will take drug for a lot of people then enter into a tender at very cheap prices. I mean that the price given in a tender is very low but when the medicine is sold in the market, it is expensive." **R1**

"By selling medicine through tenders I achieve lots of benefits. I make my product known to people even if I do not make lots of profit. A tender means that I give supply bulk quantities solely to one procurer, which is a governmental warehouse. This spares me transportation expenses that would otherwise be spent on transportation to the various parts of the country. It spares me marketing and medical care costs. In addition, manufacturing costs for me in tenders are lower than usual." **R2**

"One pack costs the manufacturer one Jordanian Dinar and is sold in pharmacies at JD24. In tenders, it is sold at 2.5 and still the company is making profit." **R3**

*"This also means that the 80% is too much exaggerated. To give you a quick taste, compare the prices with those given in tenders. Sometimes, such prices in tenders are even as low as 50% of the price sold to people."***R4**

Theme 13: Generic substitution was not welcomed

The participants did not welcome the introduction of a generic substitution policy as it will only benefit the pharmacists not the patients. Furthermore, a generic substitution policy will put more pressure on local manufacturers to increase their bonus to manipulate the market.

"We here come back to the bonus issue. The one who gives you more is the one whose products you sell more. It will not make a difference in price for people. People will not benefit at all." ***R1***

"This is a mistake because it will add to the power and control of the pharmacist. It will only benefit the pharmacist." ***R2***

*"I do not agree with generic substitutions except after consultation with the doctor or after taking the permission of the patient. Otherwise, if a pharmacist is given the full authority to substitute the prescribed medicine without referring back to the doctor, the substitution will likely be made in accordance with the interest and profit of the pharmacist rather than the interest of the patient."****R3***

"In this case, the pharmacist will negotiate with companies to get the largest possible bonus. Such medicines are then replaced just for the benefit of the pharmacist and not to serve the interest of the patient." ***R4***

Theme 14: Generic prescribing was not welcomed

Generic medicines are generally marketed under the non-proprietary name or can be marketed as branded generics,[192] as in the case of Jordan where 97% of all generic medicines are branded.[134] When participants were asked about the introduction of generic prescribing using International Non-proprietary Name (INN), the idea was not welcomed as interviewees did not feel it will benefit the patients but only the pharmacists, with a detriment effect to the local industry which relies on branded generics.

"This will be fatal for the Jordanian industry. The main feature of this industry in Jordan and in the Arab world is that they are branded generic." ***R2***

*"I do not think it works. At least this has never been tried out in Jordan. If you do that, you are giving full authority to the pharmacist. Perhaps it works in other countries but definitely not in Jordan."****R3***

"Not in the interest of the patient. The pharmacist will replace the medicine that brings him the highest profit gained by the bonus." ***R4***

The policy maker representative accepted it in principle, but emphasised that it needs to be supported by an awareness campaign to change behaviours.

*"This unfortunately needs awareness raising campaigns and public to be well informed."****R1***

One interviewee felt that inpatients and the public insured sector may benefit from INN prescribing.

"The public sector and in-hospital patients may benefit from that." ***R4***

Theme 15: The registration of two drug names was not agreed

The suggestion of registering the same drug in two different names; one for the local market and the other for export, was not accepted as the regulator viewed this as supplying false information. The local manufacturers' representative was concerned that this practice might affect their credibility in the exportation markets.

> *"I cannot provide any false information. The information I give out must be true because we are the Ministry of Health and must be a source of credibility."* ***R1***

> *"I cannot see anything wrong in that. Each product will have its own invoice and price. But I am not sure of the companies or exportation markets will accept such a practice. The world is small and people will know about it. I do not know if anywhere else in the world such a practice is followed."* ***R2***

Sub theme 1: The Jordanian pharmaceutical industry is important for economic stability and employment

The Pharmaceutical industry in Jordan is important for its economic stability and unemployment reduction.

> *"What you need is a country that has strong economy where people can work and buy the medicine at moderate prices."* ***R2***

> *"The pharmaceutical industry in Jordan is one of the most important industries. It serves Jordanians in terms of numbers of employees there and the benefiting families. We need to consider also the high power supply costs in Jordan compared with those in the region. Pharmaceutical factories also serve the local community."* ***R2***

Sub theme 2: The industry in Jordan is a private business

Jordan pharmaceutical companies are private, not governmental sector so are driven by profit.

> *"We also have to remember that pharmaceutical companies in Jordan are private and not public companies as in the case of Egypt and Syria. Our companies are profit-seeking companies."* ***R2***

Sub-theme 3: Imported generics have low prices

Regarding imported generics, their prices are based on their country of origin or ex-factory prices plus wholesalers and retail profit margins. This achieves very low prices as usually the country of origin price is very low because of the strict price control in other countries.

> *"The generic that is imported from abroad is less than 80% because in the country of origin, control departments control prices but in Jordan almost all generics' factories price at an 80% basis."* ***R1***

The use of ex-factory prices may stop wholesalers' import medicines due to low profits.

> *"This makes them depend on the ex-factory price. This makes the price considerably low. Some companies refuse such a price and deprive the Jordanian people from such medicines."* ***R4***

Sub-theme 4: Lack of R&D

The high prices of local products should initiate/motivate the R&D of life saving drugs; e.g. anti-cancer, anesthetics etc., but it doesn't.

> *"We agree that local industry should be supported but lots of medicines are not available because the local industry cannot produce them. What is the added value of the local industry? A drug like ranitidine has more than twenty generics but the local industry has no anaesthetic medicine. You cannot find life-saving drugs such as anti-cancer drugs because our local industry looks for the easiest produced ones and the most profitable."* ***R4***

Sub-theme 5: Problems in the application of the policy

When the originators' prices decrease internationally, this decrease is not reflected in Jordan, the prices stay the same as there are no frequent pricing revisions.

> *"The prices of such originators are decreasing worldwide but this decrease is not reflecting on a decrease in Jordan. The problem is in application."* ***R4***

Sub-theme 6: Locally packaged medicines are priced as locally produced generics

Although some medicines are imported from abroad at very low prices and are only packaged with new leaflets in Jordan, they are priced as generics which are manufactured completely in Jordan at 80% of originator price.

> *"Also there is contractual importation where medicines are imported from abroad at very low prices then are packed only in Jordan and their leaflets are printed locally. They take 80% of the price of the originator"* ***R4***

4.5 DISCUSSION:

Although the income per capita is much lower in Jordan (almost 7 fold less than the UK),[111] generic drugs are three times more expensive than the equivalent prices of the same drugs in the UK. Furthermore, originator medicines are 1.5 times more expensive in Jordan compared to the UK. Additionally, the difference in prices for many drugs was significantly high. For example, the Jordanian price of misoprostol originator tablets was around 19 times the comparable UK price. The price of ranitidine originator in Jordan was also more than seven times the UK price, and for the lansoprasole originator it was around 6 times the price of the UK. Moreover, the average price of pravastatin and amlodipine generics was more than eight fold higher than the UK price. The average price of omeprazole, citalopram and fluoxetine generics were around 10 fold higher than the comparable UK price.

The results from this chapter were consistent with a previous study conducted by the researcher in which the prices in Jordan were higher than those of the UK for both originator and generic product.[126] Moreover, the WHO pricing survey [4] found that the prices of medicines in both the Jordanian public and private sectors were higher than the international reference price.

The qualitative study provided rich and novel data about medicine prices and policies in Jordan, which is essential knowledge for improving access to affordable medicines and for justifying the high prices of medicines in Jordan compared with the UK. As identified by the thematic analysis of the interviews conducted; the pricing policy is believed to be the

root cause for the high prices of generic and originator medicines in Jordan. This was consistent with previous studies that considered the pricing policy as the main factor influencing the prices of medicines all over the world.[117,127-128]

From the results obtained in chapter 3 and as emphasised in the qualitative study, it is evident that while the prices of originators decreased internationally, they stayed the same in Jordan. This is believed to be due to the lack of frequent pricing revisions by the regulatory body; JFDA. Moreover, the findings from the price comparisons showed that the differences between some of the prices of originator and generic medicines were less than 20% in Jordan. This is due to the fact that some originator prices decreased, however this was not reflected in the prices of generics. The current policy allows for local generic manufacturers to price their product up to 80% from the originator price.[15] Therefore price revisions should be conducted more frequently to ensure that.

Nevertheless, the 80% ceiling achieves high profits for local manufacturers, considering the low production costs of generic medicines which have no R&D costs to recover.[43] This was admitted by a local manufacturer in the interviews. Moreover, selling through tenders and high bonuses emphasise that the 80% ceiling is too much exaggerated as revealed by the participants. This suggests that the 80% ceiling should be revised.

The results from this study were similar to these reported by King and Kanavos [193] in 2002. They found that generic medicines are in general 20-90% less expensive than the originator medicines. In Jordan, the expected patient saving by using generic medicines instead of originators was 32% up to 74%. The results showed that the average prices of generic medicines in Jordan were 30% less than their equivalent originator. Although, it would have been expected that the average saving from using generics will be 20% (based on the pricing policy), the 30% average calculated could be due to imported generics which are priced at a lower price parallel to their country of origin price. The saving observed could also be due to the extra 3-5% decrease in price from the 80% ceiling imposed by the pricing policy applied by local manufacturers as outlined by one of the interviewees under theme 8.

In the UK, the expected calculated average saving by generic use was higher than that in Jordan, especially when we took out the outlier, the median price difference between the generics and the originators was -72.27% and the average saving was 54.96%. This

calculated saving explains why the majority of medicines are prescribed and dispensed generically in the UK [47,49].

The saving calculated in both countries could have been even higher if the lowest priced generic was used to calculate it rather than the average price of generics. A recent study carried out in several countries, including Jordan, estimated that an average savings of 9% to 89% could be made by an individual country by substituting some originator brands to the lowest-priced generics.[194] It was found that if 11 originator medicines were switched to the lowest available generics in Jordan, the estimated saving could be 56%.[194] When the extra saving from using the lowest-priced generics for all the drugs studied in the cardiovascular system was calculated in Jordan, an extra saving of 6.86% was identified (an increase from 32.71% saving when using the average generic price compared to 39.57% when using lowest priced generic) (Table 4.5). Nevertheless, the proposal of introducing generic substitution and generic prescribing policies were opposed by the interviewees.

Table 4.5 Expected saving by using lowest price generic available

Class	Active Ingredient	% Expected saving by using mean price generics	% Expected saving by using Lowest price generics
Antiarrhythmic	amiodarone	-28.24%	-28.34%
Beta blocker	atenolol	-61.71%	-66.95%
	bisoprolol	-1.06%	-15.02%
Alpha blocker	doxazosin	-46.31%	-54.16%
Angiotensin converting enzyme inhibitor	captopril	-23.93%	-25.66%
	enalapril	-48.31%	-58.90%
	fosonopril	-20.20%	-20.41%
	lisinopril	-47.97%	-63.53%
CCB	amlodipine	-33.33%	-33.13%
Statin	simvastatin	-11.83%	-19.36%
Fibrate	bezafibrate	-43.20%	-44.55%
	gemfibrozil	-26.43%	-44.79%
Average Expected saving		**-32.71%**	**-39.57%**

The interviewees welcomed the suggestion of introducing categories for pharmacy profit margin according to the price of medicines; for example if the medicine price is low the percentage profit of selling it is more compared to the expensive medicine. Therefore, pharmacists will have more of an incentive to sell cheaper medicines, instead of the expensive ones, to the public. The current fixed profit margin may make pharmacists eager to sell expensive medicines which negatively affect patients in Jordan.

CHAPTER FIVE

USE OF GENERIC MEDICINES IN JORDAN: A STUDY OF PATIENTS', PHARMACISTS' AND PHYSICIANS' PERSPECTIVES

5.1 INTRODUCTION:

The high health care expenditure on pharmaceutical products is becoming a challenging issue worldwide.[195-196] In 2007, the expenditure on drugs in Jordan exceeded US$ 700 million, which accounted for around one-third of the national health care budget. These costs are believed to be higher than most countries with a similar income level as Jordan.[197]

The use of cheaper generic medicines is often promoted as a measure to reduce the health care expenditure on pharmaceutical products, thus providing savings to patients as well as governments.[193,198] Generally, the generic medicines are 20-90% less expensive than the innovator medicines.[193] Moreover, as identified by the comparison in chapter 4, the expected patient saving by using generic medicines instead of originators in Jordan was 32% up to 74%. The median saving in Jordan was 30.65% compared to 71.43% in UK. The average savings were 32.68% and 43.54% in Jordan and UK respectively.. This increased to 54.96% in the UK when one outlier was removed. However, the saving calculated in both countries would have been higher if the lowest priced generic was used instead of the average price of generics used, as highlighted in chapter 4.

Public and private third party payers and healthcare authorities increasingly encourage or mandate the use of generics through measures such as generic prescribing and generic substitution.[199,46,58,127,60] It has been estimated that €25 billion (more than $30 billion) is the annual saving made by European patients and health care systems by using generic medicines.[193] Furthermore, it was reported that the use of generic medicines saved American patients, taxpayers, federal and state governments and other payers $193 billion in 2011 alone and around $1.07 trillion over the period from 2002 to 2011. [200] As highlighted in chapter 4, a WHO study carried out in several developing countries, including Jordan, estimated that an average savings of 9% to 89% could be made by an

individual country by substituting some originator brands to the lowest-priced generics.[194] In addition, the report stipulated that the saving in Jordan could be 56% if only 11 originator medicines were switched to the lowest available generics.[194]

In the USA, once a generic medicine has been approved by the Food and Drug Administration (FDA), this medicine can be dispensed by pharmacists as a substitute to its reference prescribed originator medicine, provided the generic medicine has the same clinical efficacy as well as safety.[201]

In 2003, pharmacists in Finland were obligated to switch a prescribed medicine to the least, or close to least, expensive medicine (usually the generic equivalent) provided that the prescribed medicine was not within a certain defined limit (price corridor) of the maximum price, and neither the prescriber nor the patient objected to the substitution. The price corridor is reviewed every 3 months on the basis of price notifications submitted by pharmaceutical companies.[202-203] The total savings generated during the first year of implementation amounted to 88.3 million euros.[204]

In the UK, it was reported that more than 83% of the prescriptions in 2007 were written generically,[47] thus making the issue of generic substitution less pressing. In addition, pharmacists have an economic incentive, through supplier discounts, to dispense generic medicines.[48] In England, 68.9% of all prescription items were dispensed as generic medicines in 2011.[49]

In Canada, the IMS Health reports showed that 54% of all prescriptions were dispensed using generic medicines in the year 2009. This made a savings of $4 billion to Canada's health care system. Higher figures were reported in the United States, according to the IMS Health reports, generic medicines were dispensed in 75% of all prescriptions in the USA.[205]

In 2002, a circular from the Jordanian Ministry of Health required doctors in public hospitals and health clinics to prescribe generically. However, if a brand name is prescribed, the patient gets the formulary drug anyway, unless their physician builds a case and receives special permission to have the brand name dispensed. Furthermore, private health insurance companies encourage doctors to prescribe the lowest priced generic.[105] On the other hand, in the private sector there is no requirement or encouragement to

prescribe generics. Furthermore, under the current Jordanian legislation, pharmacists are not permitted to make any change or substitution to prescriptions, unless the pharmacist contacts the prescriber and requests permission for the prescribed originator medicine to be substituted for an alternative generic medicine.[135]

Despite the financial benefits from using generic medicines, there are still debates regarding generic substitution by patients as well as prescribers, with regards to its effect on patients' clinical outcomes.[206-208] A German study found that half of the primary care patients are sceptical about generic substitution, and 13% of the patients reported that they had experienced new adverse reactions.[209] On the other hand, another study revealed that 61% of Slovakian patients had positive views regarding generic medicines.[210] The views in the former study were expressed by patients who were more than 60 years of age, chronically ill, and/or without higher education. In the latter study the respondents were predominantly aged 30 years or younger. This indicates that patients' socio demographic characteristics; such as educational level, income and age may influence people's opinions of generic drugs.[211]

Other factors that may influence patients' attitudes towards generic medicines are believed to be the physicians' prescribing behaviour and their preferences for a particular originator brand, or their bias against generics.[212] Moreover, the information given by a prescribing physician on generic substitution was also found to be a main driver that influences patients' beliefs about generic medicines and their consumption.[209,213]

The prescribing behaviour of physicians is considered to be crucial for generic utilisation as they determine whether their patients need branded drugs or generic drugs.[214] A generic medicine may not always be suitable for the patient.[215] Several factors may play a significant role in influencing the physicians' prescribing behaviour such as the "trust" and the "quality image" of the pharmaceutical company.[216] Physicians' prescribing behaviour can also be influenced by pharmaceutical companies through a variety of incentives such as high-end education programs or even some cash payment for prescriptions.[217] In addition, free samples and gifts that include financing for domestic and international conference participation, travel and accommodation, medical education, meals, honoraria and small gifts like pens can also influence prescribing.[218-219] However, one cannot state that physicians prescribe only on the basis of the rewards that they receive from the company, but the rewards certainly help physicians to remember the

company brands.[218-219] Therefore, these incentives may indirectly affect the patients, by encouraging them to use higher priced originator-branded products instead of equally effective, lower-cost generics.[220] One strategy to encourage the utilisation of generic medications is by generic prescribing, where physicians write prescriptions using the INN.[221-223]

It was claimed that a patient's socio-economic status may be a major factor in the physician prescribing decision.[224] Furthermore, patients' requests and preferences play a vital role in their prescribing behaviour. According to previous research, lack of physicians' compliance with their patients requests results in less patients satisfaction with their physician's visit.[225-226]

Although patient perceptions may play an important role in medication selection, previous research revealed that patients often do not communicate with their physicians about their medicine preference and the cost of medication. Furthermore, several studies found that the high out of pocket-costs can be a significant obstacle to medical adherence with prescription medication regimens.[227-229] In Jordan, over 80% of the cost of medicines purchased by the public is funded through out-of pocket payments.[4]

Previous studies showed that patient willingness to accept a generic medicine is a core requirement to facilitate the uptake of generic medicines.[230-231] In addition, physicians and pharmacists play an important role when patients choose between branded or generic drugs.[201,232-233] Patients can request generic medications at the point of the clinical encounter or at the time of dispensing of the medication at the pharmacy. [234] Therefore, efforts to promote generic substitution practice should be targeted first and foremost at time of prescribing as well as dispensing.[235]

Globally, physicians are much more sensitive to arguments about a drug's efficacy than about its price.[165,236] The effect of price and cost of medicine was found to be insignificant in physician prescribing behaviour,[237] as they do not bear the full cost of the prescribed drug, or they possess limited information about the cost and prices of medicines.[238-240]

An efficient source of information about the cost of medicines can be achieved through an electronic prescribing (EP) system, where prescriptions are generated by physicians and

transmitted electronically to pharmacies through a secure network.[241] This involves direct computer-to-computer transmission of prescriptions.[242] Not only can EP reduce health care costs by avoiding adverse drug events and substitution to less expensive medicine, but it can also enable the prescribers to check patients' health plan or insurance coverage at the point of care. Additionally, it offers physicians a powerful tool to manage their patients medication in a safe and efficient way. EP can enhance patient safety and medication compliance, improve prescribing accuracy and efficiency, decrease pharmacy costs, reduce phone calls between pharmacists and physicians, reduce data entry, expedite prescription refill requests compared to paper-based prescribing and eliminate handwriting interpretation errors.[243-244] It was reported that 7000 patients die every year in the US due to medication errors, including errors caused by illegible handwritten prescriptions. As a result, the use of EP was promoted.[245-246] In another study which was conducted in a UK hospital, there was a significant reduction in both pharmacists' interventions and prescribing errors following the introduction of EP. Interventions were reduced from 3.0% on all medication orders to 1.9%, and errors from 3.8% to 2.0%.[247] Moreover, a previous study found that using an EP system increased physicians' generic substitution rate by 15% and increased generic prescribing by more than 8%.[248]

In Jordan, despite the continuous increase in pharmaceutical expenditure, a pharmaceutical policy focusing on the promotion of generics utilisation has never been developed. In order to implement such a policy, all stakeholders should be involved. Therefore, this chapter aims to explore Jordanian patients' and pharmacists' perceptions toward generic medicines, as well as to evaluate their opinions regarding generic substitution. Moreover, this study investigated physicians' perception and attitudes toward generic medicines and generic substitution, and it examined factors that affect their pattern of prescription and their opinion regarding the future introduction of EP in Jordan. The findings from this study would provide baseline data for the introduction of a robust generic policy and eventually the use of more efficient measures to control pharmaceutical expenditure.

5.2 METHODOLOGY

5.2.1 GENERAL METHOD

In these cross sectional studies, three questionnaires were carried out to collect data from Jordanian patients, pharmacists and physicians. The participation in these studies was strictly voluntary and the informed consent of the participants was obtained. The anonymity of the respondents was preserved in the study, as the names of the participants were not included.

Data was collected from 5th June 2012 to 15th August 2012. All the collected data were entered into PASW® 18.0 for descriptive analysis using descriptive statistics techniques such as, frequency and cross-tabulation and inferential statistics using chi square tests.

This study was approved by the Research Ethics Committee of Kingston University, London.

5.2.2 PARTICIPANT SELECTION AND QUESTIONNAIRE DESIGN

5.2.2.1 PATIENTS STUDY

Patients were targeted by visiting private and public clinics, private and public hospitals, community pharmacies and The National Centre for Diabetes, Endocrinology & Genetics in Jordan. The researcher was available on site if the responders needed any clarification at the time of the study.

The questionnaire was tested for content validity by two experts. It was further revised after pilot testing with 25 patients. Patients were given an information sheet translated to the Arabic language by certified translator which explained the purpose of the research undertaken. The questionnaire was also translated to the Arabic language by a certified translator (Appendix 7-10).

The questionnaire used consisted of three sections. The first section gave a simple definition of originator and generic medicines with examples. The second section evaluated the preferred prescribed medicines and the perceptions regarding originator to

generic substitution and the costs of medicines in Jordan. The last section characterised the respondents' demographics.

The responses were framed in a four point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) questions.

In this study, the sample population was Jordanian patients with chronic medical conditions. As the population size is undetermined and according to the mathematics of probability which proved that the population size is irrelevant unless the size of the sample exceeds a few percent of the total population you are examining. This means that a sample of 500 people is equally useful in examining the opinions of a country of 10 million as it would a city of 100,000 or a group of 1,000. Population size is only likely to be a factor when you work with a relatively small and known group of people.[249] Therefore 500 questionnaires were distributed. From the 500 questionnaires which were distributed, 400 questionnaires were completed and included in this study which gave a response rate of 80%. The participation of patients approached was strictly voluntary and their informed consent was obtained. The anonymity of respondents was preserved in the study, as the names of the participants were not included.

5.2.2.2 PHARMACISTS' STUDY

This study targeted Jordanian pharmacists working in community pharmacies in both affluent and less-affluent areas of Amman.

The questionnaire was tested for content validity by two experts. It was further revised after pilot testing with 10 community pharmacists. There are four sections in the questionnaire. The first section evaluated the knowledge of generic medicines and the perceptions regarding originator to generic substitution. The second section explored the pharmacists' current generic substitution practice. The third section explored the pharmacists' views of future implementation of a generic substitution policy. The last section characterised the respondents' demographics.

The responses were framed in different types such as single answer and multiple answer closed questions, and four point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) questions.

In this study, the population was identified as Jordanian registered community pharmacists. The sampling unit was community pharmacy and the sampling frame was a list of community pharmacies in Amman (N=1252), which was obtained from the Jordanian Pharmaceutical Association. A representative sample of 294 was calculated from the population (N=1252) with a 5% margin of error and 95% confidence level. In order to reach the representative sample size of 294, five hundred pharmacies were randomly selected to participate in this survey by using Microsoft Excel randomization software.[250]

Invitation letters along with the questionnaire were given to each pharmacy and the questionnaires were collected within one week time (Appendix 11, 12). When the representative sample size (294 questionnaires) was reached, data collection stopped (response rate was 58.8%).

5.2.2.3 PHYSICIANS STUDY

This study targeted Jordanian physicians working in both private and public sectors.

The questionnaire was tested for content validity by two experts. It was further revised after pilot testing with five physicians. There are four sections in the questionnaire.

The first section characterised the respondents' demographics. The following section evaluated the prescribing behaviour of the responding physicians. The third section explored the physicians' perception towards generic medicines. The last section measured the physicians' opinion regarding the issues pertaining to the use of generics in Jordan. The responses were framed in different type such as single, multiple (participants were allowed to choose more than one answer) and four point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) questions.

According to the Jordanian Medical Association, the entire sample population is 17000 physicians; a representative sample from the population (N=17000) based on a 5% margin of error and a 95% confidence level were 376. Five hundred physicians were randomly selected to participate in this survey by using Microsoft Excel randomization software.[250] Invitation letters along with the questionnaire were given to each physician and the questionnaires were collected within one week time (Appendix 13, 14). When the representative sample size (376 questionnaires) was reached, data collection stopped (response rate was 75.2%).

5.3 RESULTS

5.3.1 PATIENT QUESTIONNAIRE

5.3.1.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDING PATIENTS

A total of 400 responses were received, with a response rate of 80%, the basic demographic of the responding patients is summarised in Table 5.1. The majority of the respondents' monthly income was less than 500 JD (59.25%) and the most common education level was a bachelor degree (42.5%). The respondents mostly pay the full cost of their prescription (63.25%) and have more than 6 medicines in their prescription (78.5%) (Table 5.1).

Table 5.1: Demographics and characteristics of the responders

Characteristic	*N (%)*
The monthly income	
Less than 500 JD	237 (59.25)
501-1000 JD	84 (21.00)
More than 1001 JD	79 (19.75)
Educational level	
Post graduate	79 (19.75)
Bachelor degree	170 (42.50)
College	62 (15.50)
High school	89 (22.25)
percentage paid from the prescription cost	
Do not pay at all	81 (20.25)
Pay only a percentage	66 (16.50)
Pay full cost	253 (63.25)
No. of medicines in the prescription	
1-3	29 (7.25)
4-6	57 (14.25)
More than 6	314 (78.50)
Chronic Medical condition	
Cardio-vascular diseases	122 (30.50)
Endocrine diseases	138 (34.50)
Respiratory diseases	95 (23.75)
Other chronic diseases	45 (11.25)
General health Status	
Poor	18 (4.50)
Fair	64 (16.00)
Good	142 (35.50)
Very good	121 (30.25)
Excellent	55 (13.75)

5.3.1.2 PATIENTS' VIEWS ON PREFERRED PHYSICIANS' COMMUNICATIONS

When assessing the patients' views on preferred communication with physicians, they predominantly agreed that the physician should ask them about their medicines preference (74%, n= 296) (Table 5.2). There was a significant correlation ($P < 0.05$) between patients' education level and whether or not they preferred to be asked about their medicines preferences (Table 5.3). As the education level of the responders increased their preferences to be consulted about their medicine choices increased.

Table 5.2: Patients' responses to four point Likert scale questions exploring their perception about generic medicines

No.	Survey questions/Statement	Frequency (%)			
		strongly disagree	Disagree	Agree	strongly agree
1	Physicians should ask patients about their medicines preference.	29 (7.25)	75 (18.75)	174 (43.5)	122 (30.5)
2	Patients should have the option of choosing between generic and originator.	33 (8.25)	55 (13.75)	221(55.25)	91 (22.75)
3	I don't mind the pharmacist substituting the medicine I was prescribed to a cheaper equivalent one	8 (2.00)	92 (23.00)	235(58.75)	65 (16.25)
4	I don't mind my prescribed medicines to be substituted from originator to generic. (e.g. Panadol to Revanin)	6 (1.50)	82 (20.50)	228(57.00)	84 (21.00)
5	My medicines should only be substituted from originator to generic if I request. (e.g. Panadol to Revanin)	69 (17.25)	77 (19.25)	141(35.25)	113(28.25)
6	I don't mind the pharmacist substituting my prescribed medicine to an equivalent locally produced one	3 (0.75)	84 (21.00)	204(51.00)	109(27.25)
7	I prefer to be prescribed locally produced medicines.	3 (0.75)	97 (24.25)	178(44.50)	122(30.50)
8	I prefer to be prescribed a well-known brand.	158(39.50)	131(32.75)	99 (24.75)	12 (3.00)
9	I prefer to be prescribed imported rather than local medicines.	150(37.50)	143(35.75)	87 (21.75)	20 (5.00)
10	Costs should be considered before a drug is prescribed.	3 (0.75)	81 (20.25)	220(55.00)	96 (24.00)
11	I don't mind whether my prescribed / dispensed medicine is locally produced or imported as long as it is effective.	0 (0.00)	85 (21.25)	217(54.25)	98 (24.50)

12	I prefer to be prescribed / dispensed the cheapest medicine available for the treatment of my condition.	18 (4.5)	14 (3.50)	251(62.75)	117(29.25)
13	Cost is not an issue for me as long as the medicine will treat my condition.	103(25.75)	214(53.50)	41 (10.25)	42 (10.50)
14	A more expensive medicine is a better one.	157(39.25)	99 (24.75)	69 (17.25)	75 (18.75)
15	Imported medicines are better.	154(38.50)	127(31.75)	66 (16.50)	53 (13.25)
16	Using generic medicines would provide significant saving to me.	0 (0.00)	87 (21.75)	229(57.25)	84 (21.00)
17	In general, medicine costs in Jordan are too high.	3 (0.75)	65 (16.25)	203(50.75)	129(32.25)

Most of the respondents (78%, n= 312) agreed that they should have the option of choosing between generic and originator (Table 5.2). Chi-square statistic at testing found a significant correlation ($P < 0.05$) between the educational level of the responders and whether or not they believed they should be given the choice between generic or originator medicine (Table 5.3). Patients with higher education levels tended to agree, or strongly agree with being given the choice.

Table 5.3: Statistically significant correlations calculated using Chi square test between the statements on the left with each of the demography category investigated

No.	Survey questions/Statement	Demography Criteria			
		The monthly income	***Educational level***	***Percentage paid from the cost***	***No. of medicines in the prescription***
		Chi square value			
1	Physicians should ask patients about their medicines preference.	NS	158.38**	NS	NS
2	Patients should have the option of choosing between generic and originator.	NS	163.53**	NS	NS
3	I don't mind the pharmacist substituting the medicine I was prescribed to a cheaper equivalent one	52.15**	NS	24.00**	42.03**
4	I don't mind my prescribed medicines to be substituted from originator to generic. (e.g. Panadol to Revanin)	65.12**	NS	45.95**	48.84**

5	My medicines should only be substituted from originator to generic if I request. (e.g. Panadol to Revanin)	146.12**	NS	NS	46.63**
6	I don't mind the pharmacist substituting my prescribed medicine to an equivalent locally produced one	NS	NS	NS	NS
7	I prefer to be prescribed locally produced medicines.	66.23**	NS	36.02**	55.220**
8	I prefer to be prescribed a well-known brand.	NS	NS	NS	NS
9	I prefer to be prescribed imported rather than local medicines.	16.73*	NS	16.83*	24.69**
10	Costs should be considered before a drug is prescribed.	13.83*	NS	24.07**	43.41**
11	I don't mind whether my prescribed / dispensed medicine is locally produced or imported as long as it is effective.	NS	NS	NS	NS
12	I prefer to be prescribed / dispensed the cheapest medicine available for the treatment of my condition.	21.13**	NS	NS	177.45**
13	Cost is not an issue for me as long as the medicine will treat my condition.	22.65**	NS	40.02**	68.48**
14	A more expensive medicine is a better one.	55.06**	NS	NS	142.07**
15	Imported medicines are better.	21.17**	34.72**	29.26**	134.66**
16	Using generic medicines would provide significant saving to me.	13.23*	NS	92.07**	NS
17	In general, medicine costs in Jordan are too high.	28.59**	NS	46.59**	59.87**

*:$p < 0.05$, **:$P < 0.01$, NS: non statistically significant correlations found

5.3.1.3 PERCEPTIONS ON GENERIC SUBSTITUTION

When patients were asked if they minded the pharmacist substituting their prescribed medicine, 75% responders did not mind the substitution to a cheaper equivalent (n= 300) (Table 5.2). In addition, most patients (78%, n=312) did not mind their prescribed originator medicine being substituted to a generic one (Table 5.2). There was a significant correlation ($P < 0.05$) between the patients' monthly income level, percentage cost paid for the prescription and number of medicines in the prescription and whether or not they minded their prescribed medicine to be substituted to a cheaper medicine or a generic. Patients with a lower income, pay more percentage of their medicines cost, and are on a higher number of medicines, tended to accept the substitution more. The values of chi square are shown in Table 5.3.

Most responders (63.5%) preferred to accept generic substitution only upon their request (n= 254) (Table 5.2). There was a significant correlation ($P < 0.05$) between patients' income level and the number of medicines in the prescription with their preference for generic substitution to be based on their request (Table 5.3). Patients with high income levels, and who have small numbers of medicines in their prescription, tended to agree or strongly agree with the substitution being upon their request only. However, there was no correlation with percentage paid from medicines cost and the acceptance of generic substitution upon patients' request. Interestingly, there was no correlation between the education level of the responders and their preference to be consulted prior to originator generic substitution.

5.3.1.4 OPINIONS REGARDING LOCALLY PRODUCED GENERIC MEDICINES

When assessing the patients' views on locally produced generic medicines, 75% of them preferred to be prescribed locally produced medicines (n=300) and 73.25% of the patients did not prefer to be prescribed imported rather than local medicines (n=293). There was a significant correlation ($P < 0.05$.) between patients' monthly income level, percentage cost paid for their medicines and the number of medicines in the prescription and their preference for local medicines. Patients with a low income, or more percentage cost of medicines and have higher number of prescribed medicines, tended to agree or strongly agree with being prescribed locally produced medicines (Table 5.3), whereas there was no correlation with the education level of responders and their preference for imported products or locally produced products.

When asked if imported medicines are better than locally produced ones, 70.25% of the surveyed patients disagreed (n=281) (Table 5.2). Patients with a higher education level, a lower income level, pay more percentage cost of medicines and have higher numbers of medicines prescribed, tended to disagree with imported medicines being better than locally produced ones ($P < 0.05$) (Table 3).

The majority of patients (72.25%, n=289) did not prefer to be prescribed a well-known medicine brand with 78.25% agreeing to their medicines to be substituted to a locally produced generic one (n=313).

In general, the effectiveness of the medicines is the determinant in patients preference not the manufacturing country, according to 78.75% of the responders (n=315) (Table 5.2).

5.3.1.5 JORDANIAN PATIENTS' OPINIONS REGARDING THE COST OF MEDICINES

The majority of the surveyed Jordanian patients (79%, n=316) agreed that the costs should be considered before a drug is prescribed (Table 5.2). There was a significant relationship ($P < 0.05$) between the monthly income of the patient and the percentage paid for the cost of medicine and the number of medicines in the prescriptions and their agreement. Patients with a low income level, who pay higher percentage cost of their medicines, or who have a high number of prescribed medicines, tended to agree more that costs should be considered before a drug is prescribed.

Patients predominantly (92%, n=368) preferred to be prescribed and/or dispensed the cheapest medicine available (Table 5.2). People with a low income and a high number of medicines prescribed tended to prefer to be prescribed and/or be dispensed the cheapest medicine available for the treatment of their medical condition ($P < 0.05$) (Table 5.3). However, there was no significant correlation between the percentage paid for the cost of the medicines and the preference to be prescribed or dispensed the cheapest medicine available.

Most of the patients (79.25%, n=317) disagreed with the statement "cost is not an issue for me as long as the medicine will treat my condition" (Table 5.2). A Chi-Square test of independence revealed a significant relationship ($P < 0.05$) between this response and the monthly income of the patient, the percentage they paid for the cost of their medicines and

the number of medicines they are prescribed. Patients with low income level, or pay the full cost of their medicines, or are prescribed a large number of medicines tended to disagree more with the above statement (Table 5.3).

Most of the patients (64%, n=256) disagreed that a more expensive medicine is a better one. Patients with a low income level, or who are prescribed a large number of medicines tended to disagree that a more expensive medicine is a better one ($P < 0.05$) (Table 5.3). However, there was no significant correlation with the percentage paid for medicine, or educational level, and the response to the above statement.

Patients predominantly (83%, n=332) believed that the medicine costs in Jordan are too high (Table 5.2). There was a relationship between the monthly income of the patient, the percentage paid for the cost of their medicines and the number of prescribed medicines and the agreement to this statement ($P < 0.05$) (Table 5.3). Patients with a low income level, or pay more percentage of the cost of their medicines or are on high number of medicines tended to agree more that medicine costs in Jordan are too high.

5.3.1.6 SAVING FROM USING GENERIC MEDICINES

Most of the Jordanian patients (78.25%. n= 313) believed that the use of generic medicines would provide a significant saving to them (Table 5.2). Patients with low income levels, or pay more percentage cost of medicines tended to believe that the use of generic medicines would provide significant saving for them ($P < 0.05$) (Table 5.3). However, there was no significant correlation between the number of medicines in the prescription and the belief of the saving gained by using generic medicines.

5.3.2 PHARMACISTS' QUESTIONNAIRE

5.3.2.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDING PHARMACISTS

A total of 294 responses were received, the basic demographic of the responding pharmacists is summarised in Table 5.4. The sample was almost equally distributed between male (142, 48.3%) and female (152, 51.7%). The modal age of the responding pharmacists was under 30 years with a range of under 30-60. Respondents mostly had 1-5 years' experience in practicing pharmacy. Regarding the employment position, the majority of respondents were employees. Almost the same numbers of responses were

collected from pharmacists working in the affluent area in Amman (West) and the deprived area of Amman (East) (Table 5.4).

Table 5.4: Demographics and practice characteristics

Characteristic	*N (%)*
Gender	
Male	142 (48.3)
Female	152 (51.7)
Age group, (years)	
Under 30	159 (54.1)
30-40	100 (34.0)
41-50	24 (8.2)
51-60	11 (3.7)
above 60	0 (0.0)
Practicing, (years)	
1-5	167 (56.8)
6-10	35 (11.9)
11-15	60 (20.4)
16-20	17 (5.8)
21 and above	15 (5.1)
Employment Position	
Self or part owner	75 (25.5)
Employee	219 (74.5)
Location of the pharmacy	
West Amman (Affluent)	160 (54.4)
East Amman (Deprived)	134 (45.6)

5.3.2.2 KNOWLEDGE OF GENERICS AND PERCEPTION OF GENERIC SUBSTITUTION AND PRICES OF MEDICINES

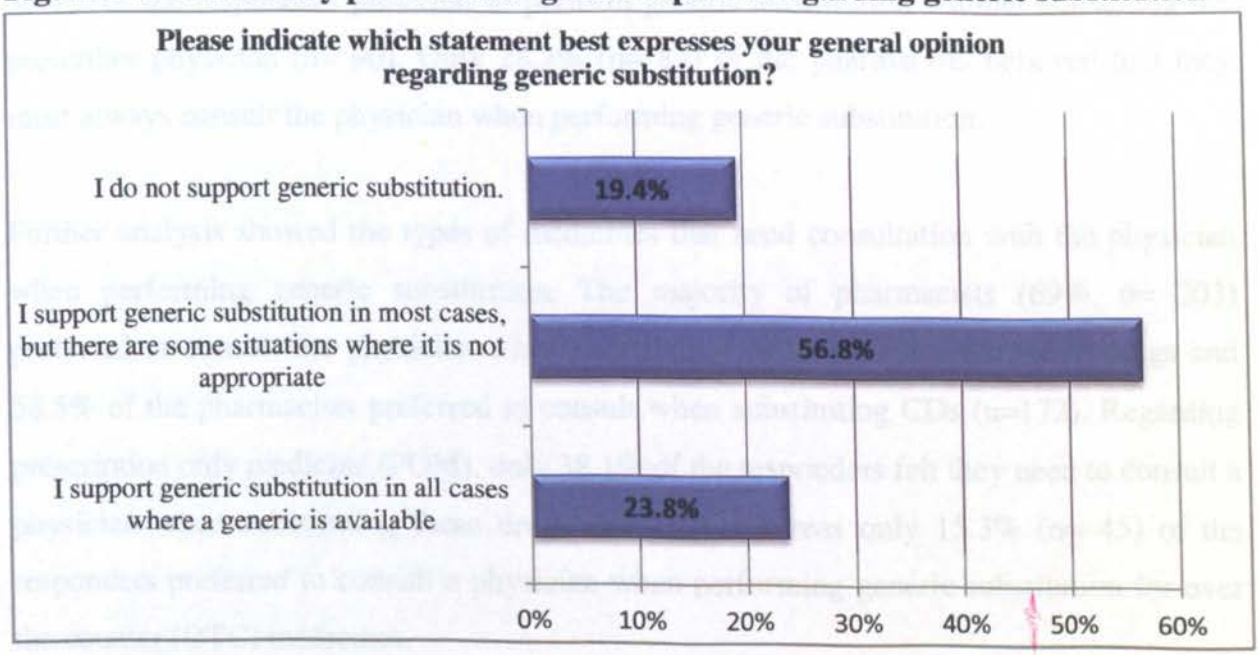
When assessing the pharmacists' views on generic medicines, the pharmacists predominantly agreed that a generic medicine is bioequivalent to its originator (87.7%, n= 258). Most of the respondents (61.9%, n= 182) disagreed that the quality of originator medicine is better compared to generics. 59.8% of the pharmacists disagreed that the generic medicines are less effective compared to originators (n= 176). The vast majority of respondents agreed that generic medicines are a cheaper alternative to the originators (90.2%, n=265). Further analysis found that 55.4% of the pharmacists perceived that the prices of medicine in Jordan does not relatively reflect the income per capita (n= 163) (Table 5.5).

Table 5.5: Community pharmacists' responses to four-point Likert scale questions exploring knowledge of generics and perception of generics' substitution and prices of medicines.

Question	Survey questions/Statement	Frequency (%)			
		strongly disagree	Disagree	Agree	strongly agree
1	A generic medicine is bioequivalent to its originator.	15 (5.1)	21 (7.1)	202(68.7)	56 (19)
2	The quality of originator medicines is better compared to generics.	73 (24.8)	109 (37.1)	97 (33)	15 (5.1)
3	Generic medicines are less effective compared to originators.	28 (9.5)	148 (50.3)	111(37.8)	7 (2.4)
4	Generic medicines are cheaper alternatives to originators.	3 (1)	26 (8.8)	221(75.2)	44 (15)
5	The prices of medicines in Jordan relatively reflect the income per capita.	70 (23.8)	93 (31.6)	100 (34)	31(10.5)

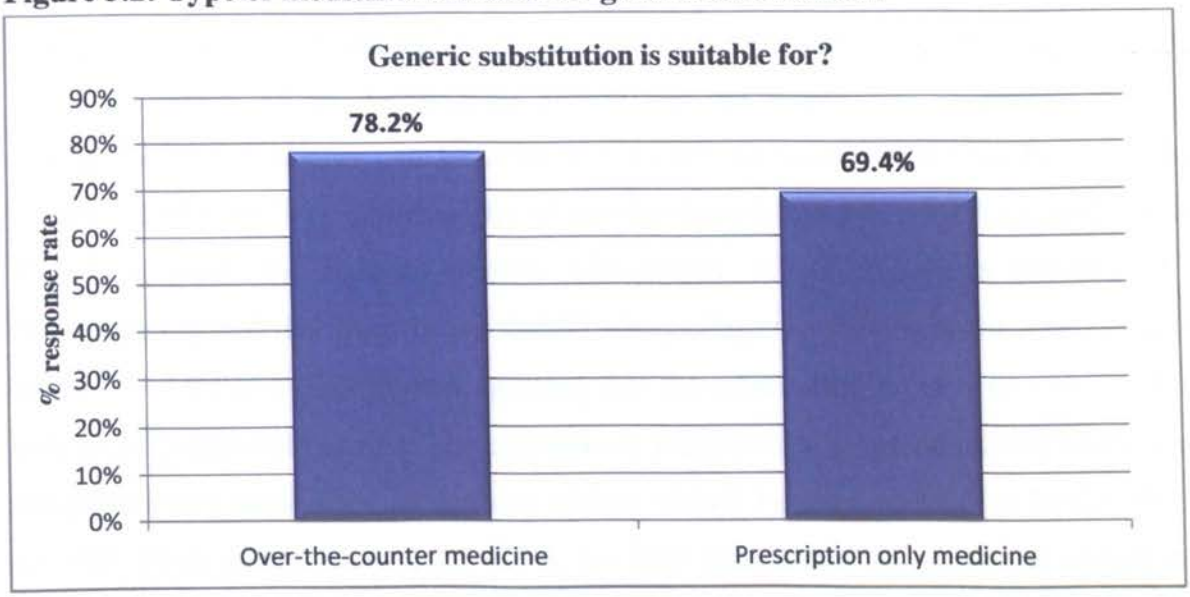
The pharmacists' opinions were further evaluated on generic substitution. More than half of the respondents (56.8%, n= 167) supported generic substitution in most cases, while 23.8% supported the substitution in all cases where a generic is available (n=70), and the rest did not support generic substitution (19.4%, n=57) (Figure 5.1).

Figure 5.1: Community pharmacists' general opinion regarding generic substitution



The pharmacists were asked about the type of medicines suitable for generic substitution and 78.2% of them believed that generic substitution is suitable for over the counter (OTC) medicines, whereas 69.4% agreed to generic substitution for prescription only medicines (POM) (Figure 5.2).

Figure 5.2: Type of medicines suitable for generic substitution



5.3.2.3 PERCEPTIONS REGARDING FUTURE IMPLEMENTATION OF A GENERIC SUBSTITUTION POLICY

When pharmacists were asked about their preference regarding the implementation of a future generic substitution policy, 41.2% of the responders believed that they only need to consult the physician when substituting certain groups of medicines (n= 121). However, 30.6% of the responders preferred to perform generic substitution without consulting the prescriber physician (n= 90). Only 28.2% (n= 83) of the pharmacists believed that they must always consult the physician when performing generic substitution.

Further analysis showed the types of medicines that need consultation with the physician when performing generic substitution. The majority of pharmacists (69%, n= 203) preferred to consult the physician when substituting narrow therapeutic index drugs and 58.5% of the pharmacists preferred to consult when substituting CDs (n=172). Regarding prescription only medicine (POM), only 38.1% of the responders felt they need to consult a physician when substituting these drugs (n= 112), whereas only 15.3% (n= 45) of the responders preferred to consult a physician when performing generic substitution for over the counter (OTC) medicines.

Two thirds (68.4%, n= 201) of the pharmacists, who answered the multiple choice question about the drivers for generic substitution, believed that they are the main driver for the generic substitution practice, while half of pharmacists (53.1%) believed that the driver of generic substitution is patient request (n= 156). The request of physician was the lowest driver as indicated by only third of the responders (35%, n= 103).

When assessing the pharmacists' views on future implementation of a generic substitution policy in Jordan, all the respondents agreed that the quality use of generic medicines among Jordanian patients can be achieved if both physicians and pharmacists worked together (100%, n=294). The majority of the pharmacists (85.4%, n= 251) agreed that they should be given the right to generic substitution. About two-thirds (69.8%) of the respondents agreed that pharmacists should always dispense the originator prescribed, with 48.3% (n= 142) of the responders agreeing that the substitution process should be allowed only at the request of patients. The pharmacists predominantly agreed that the international non-proprietary name INN prescribing system should be implemented in Jordan (90.1%, n= 265). Most of the respondents (87%, n= 256) agreed that the prescriber should write prescriptions using INN, with the pharmacist dispensing any medicine against the prescription (Table 5.6).

Table 5.6: Community pharmacists' responses to four point Likert scale questions on issues regarding future implementation of generic substitution policy

No.	Survey questions/Statement	Frequency (%)			
		strongly disagree	**Disagree**	**Agree**	**strongly agree**
1	Community pharmacists in Jordan should be given generic substitution right.	0 (0)	43 (14.6)	150 (51)	101 (34.4)
2	Generic substitution should be allowed only at patient request.	21 (7.1)	131 (44.6)	112 (38.1)	30 (10.2)
3	A prescribing system based on the international non-proprietary name INN should be implemented.	9 (3.1)	20 (6.8)	150 (51)	115 (39.1)
4	Prescribers should write prescription using the international non-proprietary name INN, and pharmacists be allowed to dispense any brand against a prescription.	6 (2)	32 (10.9)	118 (40.1)	138 (46.9)

5	Pharmacy profit margin should be variable according to your professional decision.	13 (4.4)	82 (27.9)	157 (53.4)	42 (14.3)
6	Quality use of generi c medicines among Jordanian consumers can be achieved if both physicians and pharmacist work together.	0 (0)	0 (0)	169 (57.5)	125 (42.5)
7	Pharmacist should always dispense the originator prescribed.	14 (4.8)	75 (25.5)	181 (61.6)	24 (8.2)

The pharmacists were then asked about the profit margin mark-up 68.7% (n=202) of them believed that the current profit margin should be increased, whereas 28.6% (n=84) agreed that it should remain as it is. Only 8 pharmacists (2.7%) believed that the current profit margin should be lowered (n= 8).When asked about the profit margin if generic substitution was allowed, 59.2% (n=174) of them believed that the profit margin should be increased, while 35.4% (n= 104) agreed that it should remain as it is. Only 5.4% (n=16) of the pharmacists believed that the profit margin should be lowered if generic substitution is allowed.

The measures that should be adopted if generic substitution was allowed were further evaluated. More than half of the respondents (54.8%, n= 161) believed that the generic of patient choice need to be provided, whereas 41.2% (n=121) of the responders believed that locally produced generic medicines need to be provided. One third of the pharmacists (33.3%, n= 98) believed that the cheapest medicine needs to be provided. Less than 100 pharmacists (n=95, 32.3%) supported the existence of a list of originator and generic prices to be used by pharmacists to support their generic substitution decision, with 25.5% (n=75) believing that the price list of equivalent originators/ generics needs to be provided to patients upon request. Other responses given were the need for INN prescriptions to be implemented and the supply to be based on the patient income status (5.4%, n= 16).

Some pharmacists provided additional information in relation to the topic in question, *"the current tax on drugs which is 4% should be eliminated"*. Another stated that *"there is no confidence in pharmacists by the patient as many doctors tell them not to accept any change in the prescription therefore the role of the pharmacists should be enhanced and the pharmacist should appear as highly trusted health care provider"*. The same

pharmacist stated that *"the prescribing physician and pharmacist should have continuous training through the Ministry of Health"*.

5.3.3 PHYSICIANS' QUESTIONNAIRE

5.3.3.1 DEMOGRAPHIC CHARACTERISTICS OF RESPONDING PHYSICIANS

A total of 376 responses were included, the basic demographic of the responding physicians is summarised in Table 5.7. The sample was distributed between both male (240, 63.8%) and female (136, 36.2%). The modal age of the responding physicians was between 30 and 40 years. Respondents had different years of experience in practicing medicine; the modal years of experience were from 6-10 years. Regarding the employment sector, almost the same number of responses was collected from physicians working in the private or public sectors (Table 5.7).

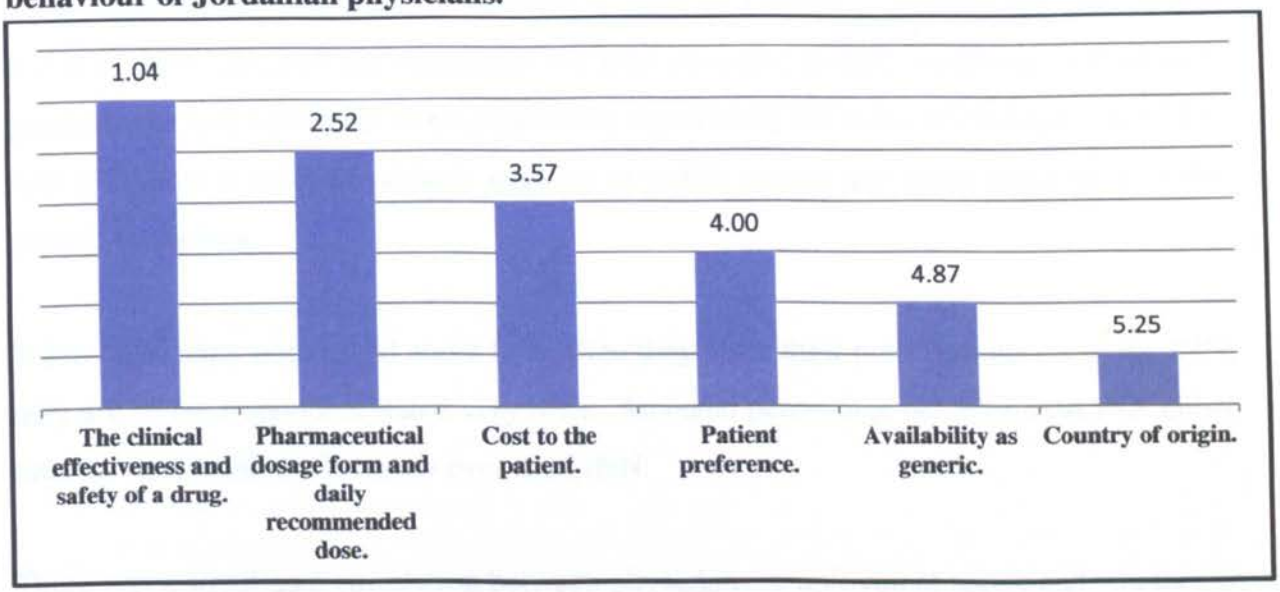
Table 5.7: Demographics and practice characteristics

Characteristic	*N (%)*
Gender	
Male	240 (63.8)
Female	136 (36.2)
Age group, (years)	
Under 30	91 (24.2)
30-40	135 (35.9)
41-50	105 (27.9)
51-60	35 (9.3)
above 60	10 (2.7)
Practicing, (years)	
1-5	96 (25.2)
6-10	100 (26.6)
11-15	75 (19.9)
16-20	70 (18.6)
21 and above	35 (9.3)
Employment Sector	
Private	180 (47.9)
Public	196 (52.1)

5.3.3.2 PRESCRIBING BEHAVIOUR

When assessing the rank of the factors that may influence physicians' decision when prescribing a medicine, the first factor was the clinical effectiveness and safety of a medicine prescribed, with a mean of 1.04. The second factor was the dosage form and daily recommended dose with a mean rank of 2.52, the cost of medicine was the third factor affecting the physicians decision, with a rank of 3.57, and the fourth factor was patient preference, with a mean rank of 4.00. The fifth rank was availability as a generic and the sixth rank was for country of origin of a medicine with means of 4.87 and 5.25, respectively (Figure 5.3).

Figure 5.3: Rankings of the means for factors that influence the prescribing behaviour of Jordanian physicians.



The physicians' prescribing behaviour was further evaluated, the majority of the respondents (86.7%) use international treatment guidelines to justify their prescribing decisions. An almost equal percentage (57.4% and 54.5%) use local guideline and local protocols or medical journals publications and online databases, respectively. Conferences and pharmaceutical sales representatives were used by 37.2% and 12% of the physicians, respectively, in order to justify their prescribing decisions. Few responders (2.7%) justify their decisions by other reasons such as their own experience and patient clinical history.

5.3.3.3 COST OF MEDICINES

The physicians were asked about the importance of cost in their prescribing decisions, 58.5% of them believed that the cost is important, 10.6% believed that the cost is highly important, whereas 30.9% of the physicians believed that the cost is not important at all.

Further analysis showed that the community pharmacists were the main source for physicians in order to get the information about cost of medicines, as mentioned by 77.1% of the responders. The second source used by 65.4% of the responding physicians, was pharmaceutical sale representatives, while the JFDA website was used by only 20.2% of physicians. Other source used was the patients according to 9.3% of responders.

5.3.3.4 CURRENT GENERIC PRESCRIBING

When assessing how often physicians prescribe generic medicines instead of originator brands in their current practice, only 1.3% of the participants stated hardly ever and 21.3% stated rarely. However, 62.8% of the physicians often prescribe generics and 14.6% of the physicians very often prescribe generic medicines instead of originator brands. A chi-square statistic was calculated to examine if there is a relation between the employment sector of the responders and whether or not they prescribe generic medicines in their daily practice. The test was found to be statistically significant; the value of chi square is 54.580 with a P value < 0.05. Physicians working in public sectors are more likely to prescribe generic medicines.

When physicians were asked about how often they write their prescriptions using the INN, only 4% of the responders stated very often. An equal percentage (43.9%) used INN either often or rarely, and 8.2% hardly ever used INN.

There was a significant correlation between physicians' employment sector and whether or not they write their prescription using the INN. The value of chi square is 28.195 with a P value < 0.05. Physicians working in public sectors are more likely to prescribe using INN.

5.3.3.5 PHYSICIANS' PERCEPTIONS ABOUT GENERIC SUBSTITUTION

When assessing the physicians' perception on generic substitution, 96% of the responding physicians agreed that the ability to perform generic substitution will ensure prompt availability of medications to the patient and that generic substitution will increase the use of locally produced medicines. Further analysis found that 92.1% of the physicians perceived that generic substitution offers a significant cost advantage to the patient. In addition, 74.7% believed that such a practice will allow pharmacists to select the most affordable drug for a patient (Table 5.8).

Table 5.8: Jordanian physicians' responses to four point Likert scale questions exploring perceptions towards generic medicines and issues pertaining the use of generics in Jordan.

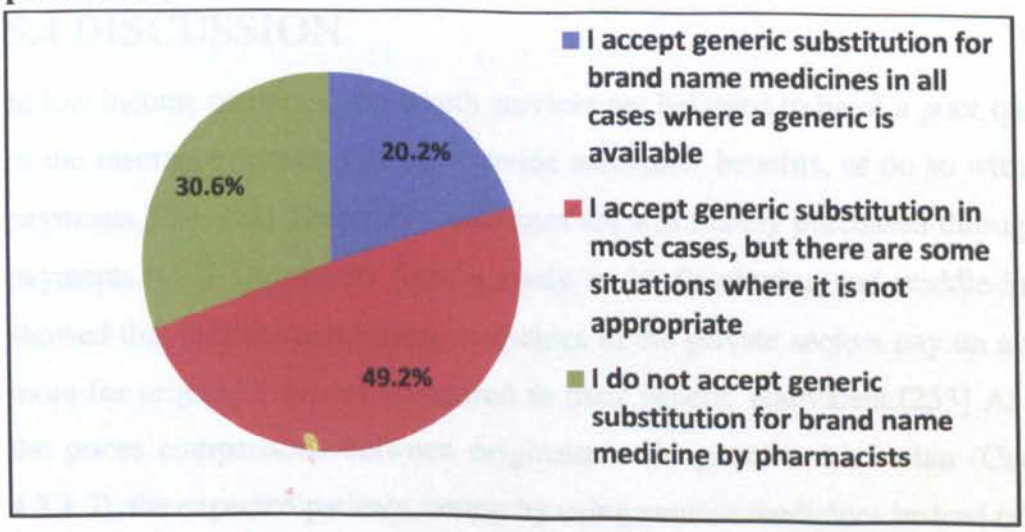
No.	Survey questions/Statement	Frequency (%)			
		strongly disagree	Disagree	Agree	strongly agree
1	Generic substitutions will increase the use of locally produced medicines.	5 (1.3%)	10 (2.7%)	276 (73.4%)	85 (22.6%)
2	Ability to perform generic substitution will ensure prompt availability of medications to the patient	0 (0.0%)	15 (4.0%)	216 (78.7%)	65 (17.3%)
3	Generic substitution offer significant cost advantage to the patient.	0 (0.0%)	30 (8.0%)	271 (72.1%)	75 (19.9%)
4	Generic substitution will allow pharmacists to select to select the most affordable drug to a patient.	5 (1.3)	90 (23.9%)	256 (68.1%)	25 (6.6%)
5	Developing a computerized system which includes important information about drugs such as: medicines interaction, contraindications and cost, would improve the prescribing process	0 (0.0%)	5 (1.3%)	180 (47.9%)	191 (50.8%)
6	Implementing an electronic prescription service would result in a more efficient prescribing and dispensing process.	0 (0%)	30 (8.0%)	241 (64.1%)	105 (27.9%)
7	Standard guidelines on generic substitution process to both physicians and pharmacists should be implemented.	0 (0.0%)	10 (2.7%)	291 (77.4%)	75 (19.9%)
8	Quality use of generic medicines among Jordanian consumers can be achieved if both physicians and pharmacist work together.	0 (0.0%)	35 (9.3%)	256 (68.1%)	85 (22.6%)
9	It is feasible to implement prescribing system based on International Non-priority Name (INN).	5 (1.3%)	70 (18.6%)	241 (64.1%)	60 (16.0%)
10	Community Pharmacist in Jordan should be given generic substitution right.	25 (6.6%)	120 (31.9%)	160 (42.6%)	71 (18.9%)
11	Generic substitution should be allowed only at patient request.	80 (21.3%)	191 (50.8%)	85 (22.6%)	20 (5.3%)

Nearly all of the responding physicians (98.7%) agreed that developing a computerised system which includes important information about drugs such as: medicines interaction, contraindications and cost, would improve the prescribing process. The majority (97.3%) also believed that standard guidelines on generic substitution for both physicians and pharmacists should be implemented. Furthermore, 90.7% agreed that quality use of generic medicines among Jordanian consumers can be achieved if both physicians and pharmacists work together. The implementation of an EP system would result in a more efficient prescribing and dispensing process, according to 92% of the responders (Table 5.8). Furthermore, the majority of the physicians (80.1%) agreed to the implementation of a prescribing system based on INN (Table 5.8).

Giving community pharmacists in Jordan a generic substitution right was agreed by 61.5% of the responders. Interestingly, 72.1% of the physicians were opposed to a generic substitution practice beingbe allowed upon patient request only (Table 5.8).

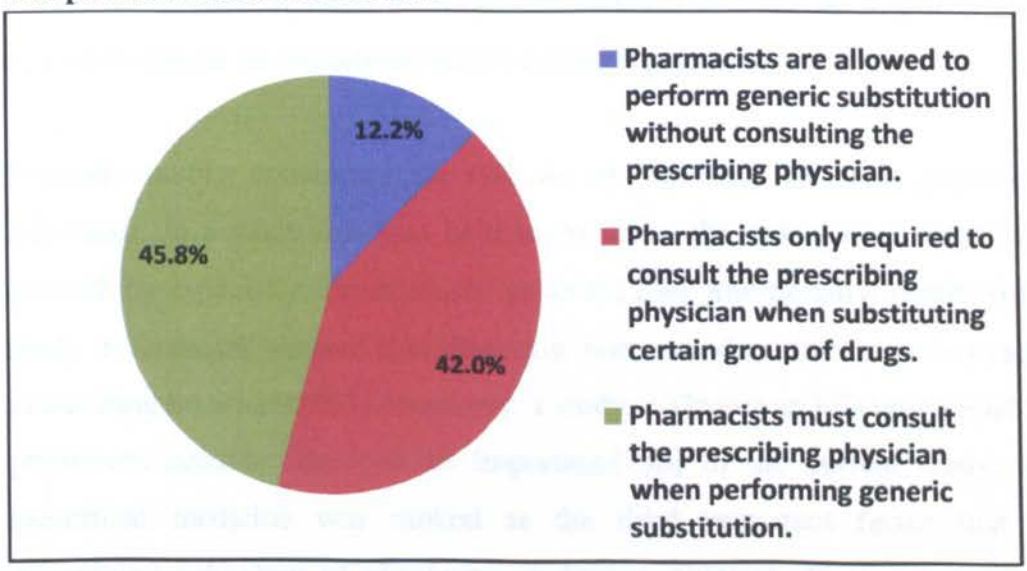
When assessing the physicians' general opinion regarding generic substitution by community pharmacists, around half of them (49.2%) accepted generic substitution in most cases as there are some situations where it is not appropriate and 20.2% accepted it in all cases where a generic is available, Interestingly, 30.6% do not accept generic substitution by pharmacists at all (Figure 5.4). There was a significant correlation between the physician' employment sector and whether or not they accept generic substitution. The value of chi squares was 11.87 with a P value < 0.05. Physicians working in the public sector tended to accept generic substitution more compared with physicians working in the private sector.

Figure 5.4: General opinion regarding generic substitution by community pharmacists



When the physicians that accepted the generic substitution in the previous question either in most or in all cases were asked about their preferred generic substitution practice, 45.8% of them believed that pharmacists must consult them when performing generic substitution. However, 42% of the responders preferred that the pharmacists only consulted them if they are substituting certain group of drugs (e.g. narrow therapeutic index). Only 12.2% of the physicians who accepted generic substitution in most or all cases believed that pharmacists should be allowed to perform generic substitution without consulting the prescribing physician (Figure 5.5). There was a significant correlation between the physicians' employment sector and the standard of practice, the value of chi square is 10.85 with a P value <0.05. By reviewing the cross table, physicians working in public sector believe that pharmacists should be allowed to perform generic substitution without consulting them.

Figure 5.5: Generic substitution preferred practice according to the physicians who accepted it in most or all cases.



5.4 DISCUSSION

In low income countries, the health services are believed to be of a poor quality, and many of the insurance schemes do not provide medicines benefits, or do so with substantial co-payments.[251-252] Therefore, medicines are still mainly purchased through out-of-pocket payments.[173] The results from a study in 36 developing and middle-income countries showed that patients purchasing medicines in the private sectors pay on average 2.6 times more for originator brands compared to their generic equivalent.[253] As identified from the prices comparisons between originators and generics in Jordan (Chapter 4, section 4.3.1.3), the expected patients saving by using generic medicines instead of originators was ranging between 32% up to 74%. However, this saving is been higher if the lowest priced

generic was used instead of the average price of all generics available. The high prices are considered as a barrier to the access to medicines.[254] In Jordan, it was reported that over 80% of the cost of medicines purchased by the public is funded through out-of pocket payments.[4] This was reflected in the population in the patients' questionnaire, where about 80% of the surveyed patients either paid full or part costs of their medicines.

In this study, the majority of the surveyed patients (83%) believed that the costs of medicines in Jordan are too high. In addition, more than half of the participant pharmacists (55.4%) perceived that the price of medicines in Jordan does not relatively reflect the low income per capita. Moreover, the costs of medicines were found to be a significant issue for about 80% of the Jordanian patients, which in turn might have a negative impact on their adherence to treatments.[227-229,255] These results were mostly reported by low income patients, patients who pay for medicines, and patients who have high number of medicines in their repeated prescriptions. Around 80% of the responding patients agreed that costs should be considered before a drug is prescribed.

Previous studies considered the cost as an important factor in physicians prescribing behaviour. In a study that was held in America, the cost was an important factor when prescribing especially for uninsured patients.[256] Additionally, results from a qualitative study in Denmark showed that drug cost was considered an important factor influencing prescribing decisions.[257] Moreover, a study in Greece and Cyprus found that 60% of the physicians consider the cost as important.[258] In the current study, the cost of the prescribed medicine was ranked as the third important factor that influenced the prescribing behaviour of physicians in Jordan. Clinical effectiveness was the first most important factor followed by the pharmaceutical dosage form and recommended daily defined dose. When the physicians were asked to rank the importance of cost in their prescribing decisions, 69.1% of them claimed that the cost is important. There was a significant association between the consideration of the cost while prescribing and the physicians' employment sector. Physicians working in the public sector were more likely to consider the cost when prescribing than their counterparts in the private sector. However, patients hardly ever communicate with their physicians about medication choices and out-of-pocket costs of medications.[211,259] Only 9.3% of the physicians reported that patient communication was the source of the medicines' cost.

The findings from this study showed that all stakeholders have high trust and confidence regarding generic medicines in general and locally produced ones in particular. More than third of the responding patients preferred to be prescribed a cheaper locally produced generic medicine rather than a more expensive imported brand medicine. Similarly, this was reflected in the physicians practice; the majority of the responders, 77.4%, claimed that they often prescribe generic medicines. However, only 47.9% of the Jordanian physicians claimed to be writing their prescriptions currently using the INN. This variation in percentage could be due to the fact that about 97% of the locally produced medicines are branded generics. This was similar to a study in Malaysia where the majority of the physicians (85.1%) claimed that they actively prescribed generic medicines in their practice.[260] On the other hand, in Greece, only one of four physicians (24.8%) prescribed generic medicines. [261]

The findings from this study also revealed that Jordanian pharmacists have positive views on generic medicines in general, in terms of quality, efficacy and safety, with 87.7% of the responding pharmacists believing that generic medicines are bio-equivalents to originator medicines.

The confidence in generic medicines was reflected in the supporting of generic substitution by all stakeholders involved. Patients predominantly (92%) preferred to be prescribed and/or dispensed the cheapest medicine available for the treatment of their medical condition. Overall, almost 80% of the patients believed that the use of generic medicines would provide a significant saving to them. The patients' acceptability of generic substitution was consistent with previous studies in Denmark, Spain and Norway where preference for the use of generics among patients was reported.[262-263] Most patients (78%) accepted their prescribed originator medicine being substituted with a generic one, with 75% and 78% accepting the pharmacist substituting their medicines to a cheaper one or to a locally produced generic respectively. This was almost the same result as a previous study in Australia where 78.5% of the patients accepted generic substitution based on the pharmacists' recommendation.[264] Another study in New Jersey, USA reported that 97% of the patients who had been offered a substitution had agreed to switch their therapy.[201] This also corresponds to a study in Finland in which 81% of the participants were of the opinion that cheaper generics were effective and 85% did not consider generics substitution as a threat to drug safety.[265] On the other hand, a Slovakian study reported that only 50% indicated a preference for a cheaper product.[210]

This confidence in generic medicines was also mirrored in the supporting of generic substitution in most cases by more than 80% of the responding pharmacists. Moreover, the vast majority of pharmacists agreed that the generic medicines are a cheaper alternative to the originators (90.2%, n=265). Similar findings were reported by Allenet *et al.* [266] in France. They indicated that 90% of the French pharmacists were in favour of the implementation of a generic substitution right.[266] Another study in Malaysia showed that more than 90% of the community pharmacists believed that they should be granted the rights of substitute.[267] However, another Malaysian study showed that community pharmacists had little confidence in locally produced generic medicines.[268] This, on the other hand, as indicated earlier, showed that Jordanian pharmacists had a positive view on generic medicines in general. In Jordan, the locally produced generics account for two thirds of the total market share.[134] The results, thus provide indirect evidence of the trust of the pharmacists in the quality of local generics, which would make the implementation of a generic substitution policy not only attractive, but would also reward the local manufacturers.

More than two thirds of pharmacists (69.4%) perceived that generic substitution is suitable for prescription only medicine which is a similar trend that was reported in the United States (69.2%).[269] However, although most of the Jordanian pharmacists supported generic substitution in most cases, they revealed that there are some situations where the prescribers need to be consulted. The two types of medicines for which the pharmacists preferred to consult the prescribing physician were those with a narrow therapeutic index or controlled drugs.

Regarding the Jordanian physicians, the majority (49.2%) accepted generic substitution in most cases but there are some situations where they believed it was not appropriate (e.g. for narrow therapeutic index drugs) and 20.2% accepted it in all cases where a generic is available. However, 30.6% did not accept generic substitution by pharmacists at all. On the other hand, the results from a previous study in America showed that 78% of the physicians supported generic substitution in most cases, 17% supported the substitution in all cases where a generic is available and only 5% did not support substitution at all.[270] It was observed statistically that there is a significant association between the physicians' acceptability of generic substitution and their employment sector; physicians who work in the private sector tended to oppose generic substitution compared to physicians who work in the public sector. This finding was similar to previous studies in which private

physicians were 50–80% more likely to oppose substitutions, as they might have stronger brand-name loyalty.[52] This could be due to private sector physicians being less restricted to participate in education and conferences paid for by pharmaceutical firms, or to perform paid assignments for them compared to public physicians as there are many rules restricting them from such participation.[271] Therefore, the private physicians' prescribing behaviour may be influenced by pharmaceutical companies through a variety of incentives such as high-end education programs or even some cash payment for prescriptions.[217] These incentives may indirectly affect the patients by encouraging them to use higher priced originator-branded products instead of equally effective, lower-cost generics.[220]

From the results, physicians use international treatment guidelines as well as local guidelines and local protocols as the main sources to justify their prescribing decisions. Medical journals publication and online databases come next and then conferences. However, pharmaceutical sales representatives were claimed to be of least importance. This contradicted the previous studies in which pharmaceuticals sale representatives were more important sources of information in New Zealand [272] Denmark [257] and in Nigeria.[273] This shows that Jordanian physicians use evidence based sources, which indicates a high competence in their professional practice.

In Jordan, it is understood that generic prescribing is used in Government clinics and hospitals. Additionally, under the private insurance arrangements, physicians are encouraged to prescribe the lower priced brands. Nevertheless, currently there are no mandatory legislations for such a practice in Jordan. In this survey, a significant percentage (90.1%) of the pharmacists were in favour of implementing a compulsory generic prescribing policy system based on the INN, with 87% of pharmacists agreeing with dispensing any medicine against the prescription. Introducing a generic prescribing policy is likely to provide additional savings to the health system and consumers. This study found that if a prescribing system, based on the INN was implemented, 80.1% of the physicians are willing to use it. This was similar to a French study, where the majority of physicians (76.2%) declared that they were willing to write their prescriptions using INN.[224] Using an INN prescribing system not only would minimise confusion but also would improve the patient acceptability of generic medicines.

Therefore, implementing a compulsory generic prescribing policy in Jordan, would not only draw the attention to the fact that there are alternatives available, but the patients would also be in a better position to choose between brands. This would have a positive economic impact to the Government as well as patients as lower priced medicines will be dispensed. This is highly important considering the low annual income per capita of 4,350 US dollars in Jordan as per 2010.[274]

It is inevitable that such policy would be damaging to the local industry, as the majority (97%) of the locally produced generics are branded generics.[134] Therefore, implementing a brand substitution policy is best suited at this stage. In fact, 61.5% of the surveyed physicians agreed that pharmacists should have the substitution right.To support pharmacists to implement the substitution policy, a formulary including information about bioequivalence between originators, generics and branded generics and their prices should be developed.

It was reported that patients' communication with physicians has a key role to promote the use of generic medicines, as their preferences are a powerful motivator to the physicians' prescribing behaviour.[224,270,275] However, patients hardly ever communicate with their physicians about medication choices and the out-of-pocket costs of medications.[211,259] Almost a third of the patients in this study believed that they should be involved in decisions regarding their medicine preference, and to have the option of choosing between generic and originator. These beliefs were reported mainly by highly educated participants. Moreover, 63.5% of responders in Jordan accepted generic substitution only upon their request. Those respondents were mainly the patients with a high monthly income, and/or have fewer numbers of medicines in their repeated prescription and /or have full medical insurance. This would indicate that these groups of patients are less sensitive to the cost of medications.

Similar findings were reported in other studies. In America, 66.7% of the patients requested substitution to generic medications from doctors or pharmacists in most cases or in all time.[211] One study in Sweden showed that the higher educated respondents were 8 times more likely to be involved in choosing and deciding the alternative medicines if available.[276] Another study from Sweden showed that 94% of the patients wanted some involvement in medicine decision making, with positive association between education and shared decision making.[277] It is believed that patients who are involved in their

medicines decision are more likely to adhere to their treatment with concomitant improvement in health.[278] Therefore, it has generally been agreed that patients should be involved in decisions making about their own health and treatment all over the world.[279-280]

Surprisingly, only 27.9% of the Jordanian physicians agreed that generic substitution should be allowed upon patient request. Thus, despite the widespread belief that medical decisions are sensitive to patients' expectations,[281] the choice of prescribed drugs appears to result essentially from the physician's own decision-making process.[282] Therefore, The Professional Medical Body in Jordan should develop good practice standards that require clinicians to involve patients in treatment choices. This could be through well-designed training courses that improve the communication skills of doctors, nurses and pharmacists with their patients.

Almost all Jordanian physicians believed that developing a computerised EP system which includes important information about drugs such as; medicines interaction, contraindications and cost, would improve the prescribing process and result in a more efficient prescribing and dispensing process. Implementing such a prescribing system not only would support improved medication adherence,[283] but also reduce costs through generic utilisation.

5.5 CONCLUSION

The findings from this study showed the positive attitude of all stakeholders towards generic medications and their high willingness and acceptance of strategies that encourage generic utilisation in Jordan, such as generic substitution, INN prescribing and EP. All these strategies would help reduce the high expenditure on drugs in Jordan which accounted for around one-third of the national health care budget.[197]

The results suggested that in order to increase the generic utilisation in Jordan, standard guidelines on the generic substitution process to both physicians and pharmacists should be implemented. Furthermore, the results highlighted that the quality use of generic medicines among Jordanian patients can be achieved if both physicians and pharmacists worked together. The adoption of a standard guideline for both physicians and pharmacists on how and when to perform generic substitution for their patients or the introduction of legislation

for compulsory generic prescribing wherever appropriate would further encourage the use of generic medicines and maintain the accessibility and affordability of medicines.[224,284-285]

From this study, it is clearly obvious that Jordanian patients have a positive attitude towards generic medicines, locally produced medicines, generic substitution, and that they prefer to be involved in their medicine treatment selection. The involvement of patients in the treatment decision making would result in more adherence and an improvement in health.

It has been noted that 97% of all generic medicines produced in Jordan are branded, therefore mandatory generic prescribing might be expected to have a negative effect on the local generics industry. Therefore, a brand substitution policy should be implemented. Such a policy should clearly state the bio-equivalence identified between the brands (i.e., branded originator and/or branded generics), and should allow for patient choices to be taken into consideration. A formulary of interchangeable medicines and their prices must be developed to guide the pharmacists' decision making when performing generic substitution. Patients' awareness, and prescribers and pharmacists training will need to take place for such a policy to be successfully implemented.

The insights gained from stakeholders will serve as a platform to guide policy makers to develop a robust generic policy in Jordan including strategies such as generic substitution, INN prescribing and EP. This would result in achieving greater clinical effectiveness and economic efficiency from drug prescribing.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 INTRODUCTION

The objective of this thesis was to research medicine prices and pricing policies in Jordan in order to recommend feasible solutions for affordable medicine prices. In this thesis, the medicines prices in Jordan were compared to the UK, the underlying causes of high medicine prices were investigated by qualitative interviews and perceptions of stakeholders towards generic medicines and means that may encourage generic utilisation were evaluated. Moreover, the factors influencing the prices in Jordan compared to UK, and the effectiveness of pricing policies were studied. The investigative research strategy adopted was a mixed methods approach of quantitative and qualitative studies, together with analyses of policy and legislation. The findings from all chapters are integrated in this chapter to better understand the researched problems and provide an evidence base for the policy recommendations and conclusions.

6.2 REVIEW OF THE RESEARCH OBJECTIVES

As outlined in chapter 1, the ultimate aim of this research was to improve access to affordable medicines for the whole of Jordan's population. However, prior to formulating recommendations for effective medicine pricing policies, a sound problem definition was required. An in-depth understanding of the determinants of patient access to affordable medicines based on the specific situation in Jordan and comparative global experience was needed and formed the basis of the chapters included in the thesis.

In chapter 2, a comprehensive review of national and international literature was provided. Moreover, the pharmaceutical policies in both countries were studied. The aim of this chapter was to get a better understanding of the drug development cost and effect of

generics entry on the pharmaceutical market and to review the current health care system and pharmaceutical policies in Jordan compared to the UK.

In chapter 3, the effect of a number of generics in a class, number of originators and time on the prices of medicines was studied. Moreover, price changes over time for each drug in the cardiovascular system, available in Jordan and in the UK were studied, in order to identify factors that may have a direct effect on prices. Chapter 3 also covered the literature on the factors that influence medicine prices.

In chapter 4, prices of medicines in Jordan were compared with the UK; a developed high income country and one of the reference countries used by Jordan pricing policy. The aim of this comparison was to provide a powerful advocacy message that the prices of medicines in a relatively poor country are the same or higher than a relatively rich country. Furthermore, the expected percentage saving for switching to generics in Jordan and in the UK was calculated. Chapter 4 also included four qualitative in-depth interviews exploring the full range of issues that arose when informed stakeholders discussed the root causes of high medicine prices and the current legislations in Jordan.

In chapter 5, data from three surveys that assessed Jordanian patients', pharmacists' and physicians' perceptions towards generic medicines in general and strategies that encourage generic utilisation were collected. These data were analysed and compared with results from other countries that already used such generic use enhancement strategies.

6.3 SYNTHESISED RESULTS OF THE RESEARCH

Integration is the key feature of mixed research, whereby the researcher mixes or integrates both the quantitative and qualitative data results and analysis in order to corroborate one element with another.

In order to explain the causes of high and unaffordable medicine prices in Jordan, the findings of all studies in this thesis were integrated. These synthesised findings are discussed below and form the basis of the policy recommendations.

6.4 JORDAN MEDICINE PRICES PROBLEM

As reported in chapter 4, 70.79% of originators were priced higher in Jordan compared with the UK. Jordanian originator prices were on average more than 1.5 fold greater than their prices in UK (+51.47%). The price differences ranged from -96.40% to +1804.14%. Moreover, 86% of the generic drugs sample studied were priced higher in Jordan compared with the UK. Jordanian generic prices were on average around triple the prices in UK (+290.4%). However the prices differences ranged from -80.66% to +997.06%.

These results emphasised that the prices are very high in Jordan, considering the difference in income per capita between the two countries (almost 7 times lower in Jordan). These high prices results were consistent with the previous pricing survey conducted by WHO/HAI in 2004, [4] which was outlined in detail in chapter 1.

6.5 REASONS FOR UNAFFORDABLE MEDICINE PRICES IN JORDAN

According to the qualitative study in chapter 4, the analysis revealed a number of factors contributing to high prices of medicines in Jordan. The policy and its application is the main reason for high price of originators and generics in Jordan compared to the UK; as it allows for local manufacturers to price their products up to 80% from originator price. However, the local manufacturers' representatives interviewed claimed that the low demand in the small Jordanian market make them request the highest prices possible as they depend on the exportation market which requests the country of origin price for price negotiation. Other themes derived included; the current policy being viewed to encourage competition between generics and originators only but not among generics; the pharmaceutical industry in Jordan is private, profit seeking; the reason of the weak pricing policy in Jordan is due to local generic industry and originator wholesalers influencing the policy.

6.5.1 DRUG STORE (WHOLESALER) MARGIN

As discussed in chapter 2 section 2.8.5, the current mark-up (15% + 4%) for drug stores (wholesalers) is very high compared with other countries such as Australia where the

wholesalers receive only 7.5% mark-up;[286] and Croatia, a developing country with similar demography to Jordan, where the mark-up margin is 8.5% only.[287] In the UK, the nominal margin is 12.5%. However, discounts may be negotiated between manufacturers and wholesalers and between wholesalers and pharmacists. The NHS list price includes wholesalers' distribution margin. [288-289]

The situation in Jordan could be exacerbated due to the facts that the prices of originators were found to be 1.5 times higher than in the UK taking into account the low income per capita in Jordan. Moreover, the price discrimination policy was not seen in Jordan; international originator manufacturers usually give huge discounts to the developing countries (price discrimination or differential pricing). A study by Lichtenberg [147] found that patients in the lowest income bracket usually pay 25% less prices for pharmaceuticals compared with patients in the high income bracket.[147] However, this was not shown in the originator prices in Jordan, as the reference countries used for the pricing of generics are those from European high income countries (chapter 2, section 2.8.1).

Therefore, the current level of the mark-up provided for drug stores for their profits; 15% and operational expenses 4%; (19% cumulative) should be reviewed.

6.5.2 PHARMACISTS' REMUNERATION

Currently pharmacists receive a fixed percentage mark up of 20% profit and 6% operational expenses (26% cumulative). This remuneration method provide incentives for pharmacists to sell high priced originators to the public rather than the cheaper equivalent generics in order to achieve high net profit. The effect of this fixed profit margin could be seen clearly in the following example (Table 6.1).

Table 6.1: Famotidine products' differences in the pharmacy profit margin.

Famotidine	Brand name	Strength and pack size	Pharmacy cost	Public price no VAT	Net pharmacy profit
Originator brand	PEPCIDIN®	20mg 30 tablets	16.10	20.29	4.19
Generic brand	AMODINE®	20mg 30 tablets	3.37	4.25	0.88

Professional responsibility of the pharmacists should include in addition to medicines dispensing, patient counselling and advice on how to use medicines correctly as well as maintenance of patients' record. This could be reflected by introducing a remuneration fee. The cost of purchasing and stocking and selling medicines vary according to the price of the drug. However, the professional practice activities are the same irrespective of the cost of drug. In the UK, pharmacists receive fees and allowances for their services. [288-289]

According to the congressional budget office study about R&D in the pharmaceutical industry,[19] the cost of drugs will continue to increase over the years as they become more selective and more difficult to produce. The cost of newer drugs reflects the R&D spending. It is believed that drug costs will increase at a rate greater than inflation rate.[19] Furthermore, as identified by chapter 3 results, the prices of 44 out of 77 classes studied in the UK and 21 out of 64 classes studied in Jordan were positively correlated with the number of years in the market. Therefore, over the years the total public price for medicines in Jordan will continue to increase, particularly as wholesalers and retailers profits mark-up is directly linked to the drug cost.

By using a fee structure remuneration, the Government can adjust the fee according to the services offered by pharmacists. Moreover, diferential remuneration fees can be applied for highly educated skilled pharmacists or for those who work in rural areas. The fee remuneration should be implemented for prescription only medicines (POM) and not for over the counter medicines (OTC). Furthermore, this fee should be for a dispensed month supply of drug for chronic medicines. For acute condition, it should only be applied for the quantity that covers the whole treatment period.

Such fee is applied in the UK, pharmacists receive a professional fee for every item dispensed including medicines and appliances. This fee is currently at 0.90 GBP per item.[290] Pharmacists can also claim a range of additional fees including fees for things such as dispensing unlicensed specials or imports, measuring and fitting hosiery and trusses and dispensing controlled drugs. [290] Moreover, the pharmacists also make their profits by the difference between the NHS list price (reimbursement price) and wholesalers negotiated discounts. [288-289]

The combination of mark-up and professional fee is most commonly used all over the world. In Australia a fixed fee of 6.42 Australian Dollar (AUD) plus mark-up of 10% for most drugs is used. However, this mark-up is reduced to 4% for expensive drugs.[291]

This fee structure remuneration plus mark-up does not mean that the patient will pay more. The patient still pay the price determined by the Government on the label. Low price items may increase slightly, on the other hand the price of the expensive item will be decreased. On the long run, as mentioned above, where the prices of new drug is increased, this method will provide significant saving.

Based on the proposed remuneration strategy,the total price of the prescription to be paid will be the sum of the pharmacy's drug cost plus a mark up margin and professional fee. The professional fee, often referred to as a dispensing fee, covers the services that the pharmacist provided. However, a study of the renumeration cost for pharmacists in Jordan should be undertaken in order to select the appropriate renumeration to be used so that professionalism can be recognised.

In order to get a better understanding, a simple example using three products is illustrated below in table 6.2. The example assumes that the mark up margin is going to be 10% and the professional fee is 1.15 JD instead of the current mark up of 20% profit and 6% pharmacy expenses (26%). For example, if the pharmacy's purchase price for a medicine is 3 JD, at the current renumeration pharmacists make 0.82 JD total profit. However, the proposed renumeration will give them more profit (1.45 JD). If the pharmacy's purchase price for a medicine is 7 JD, the current profit made is 1.90 JD, while the proposed renumeration will give 1.85 JD. For a medicine purchased at 10 JD, the proposed renumeration will save patients 0.57 JD. Thus, as the medicines cost price increase, the saving to the patients will increase. However, this might increase the prices of cheaper medicines. Thus, the proposed renumeration will reduce the price of expensive medicines, while maintaining the total profit for pharmacy. The proposed renumeration will also incentive pharmacists to sell cheaper generics.

Table 6.2: Combination of mark-up and dispensing fee pharmacists' remuneration example

Drug price to Pharmacy	Current Pharmacy Remuneration (20%+6%) mark-up	Current public price	Suggested Pharmacy Remuneration 1.15JD fee+10% mark-up	New Public Price
3JD	0.82	3.82	1.45	4.45
7JD	1.90	8.90	1.85	8.85
10JD	2.72	12.72	2.15	12.15
Total Pharmacy Renumeration	5.44 JD		5.45 JD	

6.6 POLICIES TO PROMOTE THE USE OF GENERIC MEDICINES IN JORDAN

A study of patients', pharmacists'and physicians' perspectives towards policies to promote the use of generic medicines in Jordan was undertaken.

The high cost of medicines in Jordan is believed to be the main driver for choosing generic medicines which would lead to substantial saving as identified by the findings of chapters 4 and 5. The findings from chapter 5 showed positive attitude of all stakeholders towards generic medications. They also showed the high willingness and acceptance of strategies that encourage generic utilisation in Jordan such as generic substitution, INN prescribing and EP. All these strategies would help reduce the high expenditure on drugs in Jordan which accounted for around one-third of the national health care budget.[197]

The majority of pharmacists and physicians agreed that pharmacists should contact prescribers when performing generic substitution for certain group of medication such as narrow therapeutic index drugs. This shows a good understanding of generic substitution practice from both physicians and pharmacists. Furthermore, the involvement of patients in the treatment decision making to allow them to choose the preferred medicine should be encourged. This would result in more adherence and improvement in health.

Generic substitution policy can only be implemented provided that the bio-equivalence has been established between brands, and that the regulators, prescribers, and patients agree to it. A formulary of interchangeable medicines and their prices must be developed to guide

pharmacists' decision making when performing generic substitution. The Jordanian pharmacists and physicians were generally supportive of introducing a compulsory generic prescribing legislation.

The perceptions revealed by chapter 5 will guide policy makers in Jordan in order to develop a robust generic policy including strategies such as generic substitution, INN prescribing and EP. This would result in achieving greater clinical effectiveness and economic efficiency from drug prescribing.

6.6.1 SAVING BY USING GENERIC MEDICINES INSTEAD OF ORIGINATOR BRAND

The majority of generic drugs in the sample studied in Jordan were priced less than their originator in 2010 (73%). The range of price differences between originators and generics were from +10.25% to -74.29% with an average price difference of -32.68%. In average, the saving gained by using generic medicines will be around 32.68%. In the UK, the difference between originators's and generics's prices was higher than that in Jordan, especially when we took out one outlier. The median price difference between the generics and the originators was -72.27% and the average calculated expected saving was 54.96%. Moreover, the prices of both generics and originators were less than those in Jordan. However, the reported saving in both countries was calculated using the average prices of generics available for each originator. A higher saving could be achieved in both countries by using the lowest priced generic available as highlighted in chapter 4. However, the availability of lowest priced generics in the public sector according to WHS/HAI medicine survey [4] was only 27.8%. Therefore, the Government should stock and encourage the use of lowest priced brand generics. This will benefit the patients when buying their medicines out of pocket, as usually patients seek their medicines out of pocket when it is unavailable instead of long waiting for the availability again in the public sector.

6.6.2 BARRIERS FOR GENERIC MEDICINES USE IN JORDAN

Barriers to prescribing/dispensing generic medicines in Jordan is believed to be due to different reasons such as; legal barriers where the substitution is not allowed, financial disincentives to change brands, lack of communication where physicians and patients do not communicate about the existence of generic alternatives and fear of change.

Other barriers to prescribe/dispense generic drugs could be due to the high advertising campaigns by originator companies in Jordan which may result in their high market share. This could indirectly give a false idea to physicians, pharmacists and patients that there is distictions between originators and generics. In fact, studies has shown that the amount of advertising and length of time in the market are to positively correlated with market share after patent expiry.[292]

As indicated earlier in chapter 5, the prescribing behaviour of physicians is considered to be crucial for generic utilisation as they determine whether their patients need branded drugs or generic drugs.[214] A generic medicine may not always be suitable for the patient.[215] Several factors may play a significant role in influencing the physicians' prescribing behaviour such as the "trust" and the "quality image" of the pharmaceutical company.[216] Physicians' prescribing behaviour can also be influenced by pharmaceutical companies through a variety of incentives such as high-end education programs or even some cash payment for prescriptions.[217] In addition, free samples and gifts can also influence prescribing. This can indirectly influence prescribing habits as physicians are more likely to remember such companies' brands.[218-219] This can have an indirect effect on the cost of medicines and consequent adherence of patients by prescribing them higher priced originator-branded products instead of equally effective, lower-cost generics.[220]

6.7 POLICY RECOMMENDATIONS

6.7.1 ORIGINATOR PRICING POLICY

The current basket of median countries include countries such as Italy, France and Spain which have relatively low drug prices as identified by research of Kanavos et al [179] in 2010. Moreover, it includes Belgium and New Zealand, which are similar to Jordan in terms of population and has policies in place to keep drug price to minimum. However, it also contains such as the UK, Italy, Portugal, Australia, Ireland etc. As identified in chapter 3 of this thesis, many originator companies lower their prices significantly at the end of the patent in the UK and this was not shown/reflected in Jordan as per the comparison results in chapter 4. Moreover, many policies over the world make it compulsory for the price of originator to be reduced when the first generic is registered. This is currently adopted in Saudi Arabia, where the price of originator should be reduced by at least 20% when the

first generic is registered.[191] In Austria, the price of the originator must also decrease by at least 30% within three months of the inclusion of the first generic.[293]

As identified through literature search in chapter 3, many originator multi-national companies give differential pricing to developing countries. Therefore, the Government should cancel the registeration of any products that have such differential pricing which is not reflected in its price in the Jordanian market, and investigate this by contacting these originators' manufacturers directly and comparing the originator products prices with countries that have similar demographic, development status and income as Jordan.

6.7.2 GENERIC PRICING

As discussed in details in section 2.8 chapter 2, the price of generic brand has a cap of 80% of the originator price. Many importing countries including Jordan request the price in the country of origin and this price act as a ceiling. As the domestic price is requested by importation countries and act as a reference for the price that can be obtained in the export market, this meant that local generic manufacturers had to decide between choosing the export market, or to lower their prices for the local Jordanian market. The local manufacturers have opted to request the highest price possible at 80% of the originator, as they depend on the export market rather than the local market as revealed by the qualitative study (for more details please refer to qualitative study in chapter 4). Additionally, there is no competition in the Jordanian market as all manufacturers price their medicine at the high ceiling as this forms an implicit agreement between them as identified by the qualitative study in chapter 4.

The UK pricing policy requires generics to be priced no more than the originator price at patent expiry (chapter 2, section 2.9.3). However, despite lack of clear ceiling for price, generic medicines in UK were found to be around 3 fold cheaper than Jordan (chapter 4, section 4.3.1).

In order to decrease generics' prices, the regulation should be amended to assist local industries to get a reasonable price for export. A provision could be introduced to allow registration with a price specifically for export which is higher than the local price in Jordan. Another remedy could be by changing current pricing policy to set the prices for generics on a 'cost plus profit' basis rather than the 80% ceiling based on originator price.

An alternative pricing option is to have a progressive price reduction as the number of generics increase. The first generic might enter the market at the 80% ceiling price, whereas the second generic should have a further 5% price reduction, and the third generic another 5% reduction as adopted in many countries in the world such as Saudi Arabia.[292] In Saudi Arabia the price of the first generic should not exceed 65% of that of the originator before the end of patency. The second generic is priced 10% lower than the first generic and the third is 10% lower from the second generic until the fourth generic, which is fixed at 35% of originator price before end of patency as per their 2010 drug pricing policy.[292] The price of the first generic launched in Austria should be at least 48% lower than the price of the originator brand, the price of the second generic must be reduced by another 15% compared to the first generic. Moreover, the price of the originator must also decrease by at least 30% within three months of the inclusion of the first generic. Whereas, the price of the first generic in Portugal must be at least 25% below the price of original product, and the second generic needs to reduce its price by 25% compared to the first generic.[293]

For previously registerd generics in the market, they might reduce their generic to the base level percentage that resulted every time a new generic was registered, or a flexible arrangement can be allowed for them. If they keep their prices high in the local market, this might lead to the loss in the local market share but the retention of exportation market. This might provide incentive for a new generic to enter the market through price differential which triggers competition between generics themselves and originator in the market.

6.7.3 IMPORTED GENERICS

As identified by the interview with the imported generic wholesalers representative in chapter 4, the current pricing policy is not profitable enough for wholesalers to import some important medicines that local manufacturers do not produce, this thus, keeps the monopoly for the originators. An exclusion should be introduced to allow them to price the imported generic medicines to be at least 48% less than the only originator in the market whose patent already expired. The price of originator should also be decreased by 30% at least. This policy is used in Austria.[293] This will encourage competition in the generic market, and more generics will be available in the market at lower prices and provide more saving by switching to generics. It also encourage the originator brand to lower their prices

more and more as the price difference become significant. Moreover, it will ensure availability of affordable medicines.

6.7.4 FREQUENCY OF REVIEWS

As identified from interviews and originator geneneric price comparison in Jordan presented in chapter 4, the decrease of originators' prices in the UK was not reflected in Jordan. Currently, the drug prices are reviewed two years after first time registration and every five years thereafter. It would be better to adopt a systematic review of prices on a regular basis for example annually, such a review should be undertaken by therapeutic classes so that like products are reviewed together at one time.

6.7.5 POLICY OPTIONS TO ENCOURAGE THE USE OF GENERIC MEDICINES IN JORDAN

6.7.5.1 COMPULSORY BRAND PREMIUMS

Currently, doctors in Government hospitals and health clinics are encouraged to prescribe generically. If prescribed by brand name, the patient gets the formulary drug anyway, unless their physician builds a case and receives special permission to have the brand name dispensed. Moreover, private health insurance companies encourage doctors to prescribe the lowest priced generic.[105] Under a compulsory brand premium policy, the government and the private insurance companies will subsidise only at the level of lowest generic price available in the market. If the prescriber or the patient requests other brands, the patient needs to pay the extra price difference.[294] Such a policy can lead to more competition and will provide incentives for generic manufacturers to lower their prices.

6.7.5.2 GENERIC PRESCRIBING

As mentioned earlier and in chapter 5 in details, the prescribing habits of the physicians play a major role in choosing an originator or a generic drug to be prescribed. Physicians' prescribing behaviour can be influenced by pharmaceutical companies through a variety of incentives and gifts.[217-219] Moreover, the pharmacists in Jordan get fixed percentage remuneration. Therefore, there is a financial incentive to dispense the highest price originator.

INN or generic prescribing law could be introduced to make it compulsory for physicians to prescribe generically in both the private and public sectors. This was supported and accepted by both physicians and pharmacists in Jordan. Please refer to chapter 5 for more details. Such a law might reduce the impact of physicians' preferences for particular brands.

If this law coupled with the brand premium policy, where the Governments and private insurance company only pays the price of the lowest available brand and the patient pays the difference is implemented. This would save the patients money as lower priced brands will be dispensed. This will also help the local generic industry through competition.

INN or generic prescribing would draw patients' attention towards the existence of alternatives available. However, it would not prevent the sale of the high priced generics or originators available. The INN prescribing suggestion was opposed by the local industry as they produce only branded generics as revealed from the interviews in chapter 4. Therefore, such mandatory generic prescribing might be expected to have a negative effect on the local generics industry.

6.7.5.3 BRAND SUBSTITUTION

As more than 97% of generics in Jordan are branded,[134] a brand substitution policy should be implemented instead of generic substitution. Under brand substitution, physicians will be able to prescribe by brand name and indicate on the prescription if they refuse the substitution. Moreover, local companies can still be able to promote their branded name products, which is very important for the local industry. However, such a policy can only be implemented provided that the bio-equivalence has been established between alternative brands. The physicians should have freedom to veto such substitution and patients need to agree to it.

Brand substitution and compulsory brand premium will increase the generic market share and trigger competition which could lower the prices. In addition, brand premium and brand substitution have benefits for all stakeholders involved. Originator companies need to bear in mind that the patients pay the difference above the lowest generic available price, and if the difference is large this would result in a loss of the market share. Local generic manufacturers have the opportunity to lower their prices in order to compete in this

highly competitive environment. However, some manufacturers may still depend on the export market, but in this case they will lose the Jordanian market completely.

Regarding physicians, they will still be able to veto the substitution, however, patients would still need to pay the difference. For pharmacists they can substitute between brands if both patients and physicians agree. Patients will have the opportunity to know that there is alternative cheaper medicines available and ask for the lowest priced drug.

An education campaign should be developed and targeted at physicians, pharmacists, and patients. It is important that the Government promote the use of cheaper medicines and enhances the confidence in generic medicines. This can be achieved by providing bioequivalence data that assures that switching between brands would not affect the clinical outcome.

The brand substitution process can be voluntary or compulsory. Compulsory brand substitution means that the pharmacist should dispense the lowest price brand available. This would provide greater saving to the patient, however, it would deny the element of choice. Whereas voluntary brand substitution allow patients to choose the brands and some patients will be more comfortable by paying a little more for their preferred choice. Voluntary brand substitution would give more freedom to the manufacturer to price their products.

There are no problems of introducing brand substitution legislation in Jordan due to the following reasons:

- The good quality products that are produced by local industry.
- All stakeholders (physicians, pharmacists, and patients) have positive attitude towards generics in Jordan as revealed by the results of chapter 5.
- Patients' acceptance of generic substitution by pharmacists as revealed by chapter 5 results.
- According to the patients, cost is high in Jordan and cost is a significant issue that needs to be considered, please refer to chapter 5 results.

- Pharmacists predominantly supported the introduction of a generic substitution policy (for more details please refer to chapter 5).

- When the public prescriptions are dispensed at the community pharmacy, the Government will only reimburse the lowest priced generic.[105]

Although the local manufacturers did not welcome the introduction of generic substitution as indicated in chapter 4, the brand substitution should be seen as a mean that increase their market share. Manufacturers can promote their generic brands to both physicians and pharmacists on the basis of their high quality products that are accepted internationally, their brands which are recognised for both value and quality and the fact that their products are produced in Jordan, thus are more available.

Brand substitution reduces the cost of medicines to the patients and makes all stakeholders (physicians, pharmacists, and patients) more familiar with lowest priced brands.

6.7.5.4 PRODUCT LIST

In order to introduce transperancy into the medicine selection process, a product list to inform physicians, pharmacists and patients about the available alternative brands of active ingredients and the prices is required. Moreover, information should be provided on alternative drugs to treat similar conditions. This was agreed by pharmacists in order to guide their substitution practice as seen in chapter 5.

If the use of lower price brands become implemented in Jordan, a product list must be one of the first requirement to guide prescriber and pharmacists and for patients to choose from. The list should be classified according to the therapeutic classes, similar to the BNF in the UK. In this way, physicians can examine all the alternatives available to treat the same medical condition, in order to prescribe cost effectively. As discussed in chapter 2 section 2.5, there is currently a JNDF.[104] However, this formulary should list the prices of both originators and generics and should be published more frequently as the BNF (every 6 months) and distributed to all physicians and pharmacists in both public and private sectors.

6.7.5.5 ELECTRONIC PRESCRIBING

As mentioned earlier in chapter 5, an efficient source of information about the cost of medicines is believed to be through EP, where prescriptions are generated within e-prescribing systems and are transmitted electronically to pharmacies through a secure network between physician office and the community pharmacy.[241] EP has many advantages. It reduces health care costs by avoiding adverse drug events and substitution to less expensive medicines and enables the prescribers to check patients' health plan or insurance coverage at the point of care. Additionally it offers physicians a powerful tool to manage their patients' medication in a safe and efficient way.[243-244]

Developing a computerised EP system which includes important information about drugs such as; medicines interaction, contraindications and cost, would improve the prescribing process and result in a more efficient prescribing and dispensing process. Implementing such a prescribing system not only would support improved medication adherence, but also reduce the cost through generic utilisation.[283] Jordanian physicians supported the introduction of such a system as reported by chapter 5 results.

The development of such an EP system is possible in Jordan, especially as the setting of the required infrastructure for Electronic Health Record (EHR) project database for patients in the public health sector, which is known as Hakeem program has already started in October 2009. Hakeem program will allow physicians to view their patients' records using just their national ID number. This will include comprehensive medical and surgical history and physical examinations, procedural and surgical reports, current medications, allergies, as well as in-patient and out-patient clinic visit notes. In addition, it will provide online access to lab results and digital radiological exams. This will reduce cost and improve safety, quality of care and better management of chronic diseases.[295] The EP system proposed can be an extension to the Hakeem program.

6.7.5.6 TRAINING AND EDUCATION PROGRAMS

Education programs for public and physicians and pharmacists should be developed and conducted in order to encourage the use of generics. These programs should be supported by legislation to address brand substitution, revise current generic pricing policy and develop lists that clearly outline originators and generic alternatives and prices. These programs should target the public in general and the elderly and patients getting their first chronic disease repeated prescription in particular. Private insurance companies and

consumer organisation should collaborate with the Government in these sessions to ensure that consumers and health care providers are aware about generics, and pharmacists and physicians have educational material to encourage consumers to ask if there is a cheaper generic and to give it a try.

Examples of effective means to raise public awareness include; advertising campaign, written information such as leaflets, brouchures, booklets, newspaper article, comic, TV and radio, information provided by health professional, workshops, social media, smartphone applications. The more interactive the method is, the more effective it will be.[296]

Although there is a positive trust regarding generic medicines in Jordan as showed by results in chapter 5, more assurance should be provided to physicians, pharmacists and patients about the strict regulations and monitoring process for generic products in Jordan.

There should be incentives in order to change physicians, patients and pharmacists behaviour. For patients the incentive should be through significant saving. Pharmacists' incentives could be through implementing professional dispensing fees. However, prescriber incentives may be in the form of rewards from the Government or insurance companies.

6.8 LIMITATION OF STUDY

The choice of UK was definitely a useful advocacy regarding the comparison of drugs considering the big difference in the income per capita. However, the UK is not similar in terms of health structure, pricing policy and demography. Although comparison with the UK provided useful information, a comparison with a Middle Eastern country or even Australia or New Zealand would have been best suited. However, the accessibility of data would have been difficult to the researcher. To overcome this, the analysis and recommendations provided considered policies in Saudi Arabia, Australia and other relavent countries.

Other limitation of this study was in the pharmacists' questionnaire results in chapter 5, views were limited as the majority of the responding pharmacists were employees, while only 25.5% were self or part owner. Since the country operates fixed profit margin to all

medicines, a generic substitution policy might have a negative impact on pharmacies' profit (i.e. selling originator medicine which is expensive by nature will make more profits compared to selling the alternative cheaper generics). Hence, the views of owners may have not matched the employees regarding generic substitution .

The pricing data collection was not possible before 1995 in Jordan due to lack of archives and publications. This could be a limitation as the effect of generics entry was not always possible to be identified.

In retrospect, the exclusion of 56 drugs from all body system and 16 from cardiovascular drugs based on their availability as generic in 1987, as the effect of generic launch on these originator price cannot be determined could be a limitation. These drugs might have had an influencial effect on the prices of other originators and generics within the corresponding class as competition exists between different drugs in the same class as identified from chapter 3 results. Nevertheless, competition within a class was still illustrated using other drug examples which were launched at a more recent dates.

The use of DDD could be a limitation for limited numbers of medicines such as simvastatin. As the DDD does not always mimic the actual prescribed dose; the WHO/DDD for simvastatin is 30 mg whereas the actual prescribed one is 40mg. Moreover, in this study we used the strength that is simpler and easier to match the DDD (Appendix 15). For the same example (simvastatin) we used 3 tablets 10 mg instead of combination of two (1 tablets 20mg tablet and 10 mg tablet). However, the DDD limitation did not alter the results significantly (please refer to simvastatin example in Appendix 15).

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APPENDICES

Appendix 1

جدول رقم (46) : اسعار صرف اهم العملات الاجنبية المعلنة من البنك المركزي الاردني

TABLE NO. (46) : EXCHANGE RATES OF MAJOR FOREIGN CURRENCIES ANNOUNCED BY CBJ

Units Per JD

عدد وحدات العملة لكل دينار اردني

اليورو (2) EURO (2)		فرنك فرنسي (1) French Franc (1)		مارك المانى (1) Deutsche Mark (1)		جنيه استرليني Pound Sterling		دولار امريكي U. S. Dollar		السنة Year
شراء Buying	بيع Selling	شراء Buying	بيع Selling	شراء Buying	بيع Selling	شراء Buying	بيع Selling	شراء Buying	بيع Selling	
			Period Average		معدل الفترة					
-	-	14.104	14.164	8.921	8.953	1.115	1.122	2.786	2.801	1972
-	-	13.459	13.514	8.071	8.097	1.227	1.236	3.040	3.058	1973
-	-	14.771	14.837	8.019	8.045	1.314	1.325	3.095	3.114	1974
-	-	13.351	13.405	7.657	7.680	1.397	1.409	3.117	3.137	1975
-	-	14.306	14.368	7.582	7.605	1.650	1.667	3.003	3.021	1976
-	-	14.859	14.925	7.022	7.052	1.726	1.742	3.028	3.046	1977
-	-	14.706	14.793	6.540	6.588	1.700	1.711	3.262	3.283	1978
-	-	14.124	14.205	6.086	6.124	1.565	1.575	3.319	3.341	1979
-	-	14.124	14.205	6.075	6.112	1.440	1.449	3.346	3.368	1980
-	-	16.313	16.420	6.803	6.845	1.492	1.501	3.017	3.036	1981
-	-	18.519	18.622	6.863	6.906	1.618	1.627	2.829	2.845	1982
-	-	20.833	20.964	6.998	7.042	1.811	1.822	2.746	2.762	1983
-	-	22.624	22.727	7.364	7.407	1.944	1.955	2.594	2.608	1984
-	-	22.573	22.727	7.391	7.446	1.955	1.970	2.526	2.543	1985
-	-	19.685	19.841	6.161	6.211	1.939	1.955	2.845	2.869	1986
-	-	17.668	17.794	5.288	5.319	1.797	1.808	2.946	2.963	1987
-	-	15.798	15.924	4.658	4.690	1.491	1.502	2.654	2.673	1988
-	-	11.025	11.136	3.250	3.281	1.060	1.070	1.733	1.748	1989
-	-	8.157	8.210	2.421	2.437	0.841	0.847	1.502	1.511	1990
-	-	8.237	8.285	2.422	2.436	0.829	0.833	1.466	1.472	1991
-	-	7.746	7.788	2.287	2.298	0.831	0.835	1.469	1.473	1992
1.231	1.231	8.150	8.190	2.381	2.392	0.959	0.964	1.441	1.445	1993
1.204	1.204	7.905	7.949	2.313	2.324	0.933	0.937	1.429	1.433	1994
1.091	1.091	7.095	7.132	2.037	2.048	0.902	0.907	1.425	1.429	1995
1.112	1.112	7.193	7.229	2.116	2.126	0.901	0.905	1.408	1.412	1996
1.235	1.253	8.197	8.237	2.434	2.447	0.858	0.863	1.408	1.412	1997
1.254	1.260	8.297	8.339	2.475	2.488	0.849	0.853	1.408	1.412	1998
1.320	1.327	8.661	8.704	2.582	2.595	0.870	0.874	1.408	1.412	1999
1.602	1.610	10.507	10.560	3.133	3.149	0.967	0.982	1.408	1.412	2000
1.572	1.580	10.310	10.362	3.074	3.090	0.977	0.982	1.408	1.412	2001
1.493	1.501	-	-	-	-	0.938	0.943	1.408	1.412	2002
1.246	1.253	-	-	-	-	0.862	0.866	1.408	1.412	2003
1.132	1.138	-	-	-	-	0.768	0.771	1.408	1.412	2004
1.132	1.137	-	-	-	-	0.774	0.777	1.408	1.412	2005
1.119	1.125	-	-	-	-	0.763	0.767	1.408	1.412	2006
1.027	1.033	-	-	-	-	0.703	0.706	1.408	1.412	2007
0.954	0.959	-	-	-	-	0.755	0.759	1.408	1.412	2008
1.011	1.016	-	-	-	-	0.899	0.904	1.408	1.412	2009
1.060	1.066	-	-	-	-	0.911	0.915	1.408	1.412	2010
1.010	1.016	-	-	-	-	0.877	0.882	1.408	1.412	2011
1.099	1.094	-	-	-	-	0.888	0.892	1.408	1.412	2012
			End of Period		نهاية الفترة					
-	-	14.286	14.327	8.953	8.969	1.186	1.193	2.786	2.801	1972
-	-	14.225	14.286	8.183	8.210	1.300	1.311	3.030	3.049	1973
-	-	14.045	14.104	7.576	7.599	1.340	1.351	3.165	3.185	1974
-	-	13.477	13.532	7.911	7.937	1.484	1.497	3.021	3.040	1975
-	-	14.903	14.970	7.092	7.112	1.751	1.770	3.012	3.030	1976
-	-	14.837	14.925	6.623	6.662	1.642	1.653	3.165	3.185	1977
-	-	14.205	14.286	6.192	6.231	1.667	1.678	3.401	3.425	1978
-	-	13.624	13.699	5.834	5.869	1.516	1.525	3.378	3.401	1979
-	-	14.663	14.749	6.345	6.386	1.354	1.362	3.231	3.252	1980
-	-	16.779	16.892	6.631	6.671	1.537	1.547	2.941	2.959	1981
-	-	19.084	19.194	6.734	6.775	1.747	1.758	2.837	2.853	1982
-	-	22.272	22.422	7.321	7.364	1.847	1.858	2.685	2.699	1983
-	-	23.585	23.753	7.740	7.788	2.119	2.132	2.463	2.475	1984
-	-	20.450	20.619	6.649	6.702	1.881	1.896	2.708	2.731	1985
-	-	18.657	18.762	5.643	5.679	1.971	1.983	2.898	2.915	1986
-	-	16.260	16.367	4.812	4.840	1.618	1.628	3.030	3.049	1987
-	-	12.674	12.739	3.700	3.717	1.158	1.164	2.092	2.101	1988
-	-	8.873	8.961	2.595	2.621	0.953	0.963	1.536	1.550	1989
-	-	7.651	7.698	2.249	2.263	0.782	0.786	1.499	1.508	1990
-	-	7.663	7.698	2.243	2.254	0.790	0.794	1.479	1.484	1991
-	-	7.962	8.000	2.334	2.346	0.953	0.958	1.445	1.449	1992
1.268	1.268	8.299	8.340	2.444	2.456	0.955	0.960	1.418	1.422	1993
1.160	1.160	7.593	7.634	2.205	2.216	0.908	0.913	1.425	1.429	1994
1.073	1.073	6.901	6.935	2.017	2.027	0.907	0.911	1.408	1.412	1995
1.126	1.126	7.369	7.407	2.187	2.198	0.832	0.837	1.408	1.412	1996
1.274	1.280	8.418	8.461	2.517	2.530	0.848	0.853	1.408	1.412	1997
1.205	1.211	7.924	7.962	2.363	2.375	0.845	0.849	1.408	1.412	1998
1.397	1.404	9.166	9.212	2.733	2.747	0.869	0.873	1.408	1.412	1999
1.523	1.531	9.993	10.043	2.979	2.994	0.956	0.961	1.408	1.412	2000
1.589	1.597	10.420	10.472	3.107	3.123	0.970	0.974	1.408	1.412	2001
1.342	1.348	-	-	-	-	0.877	0.882	1.408	1.412	2002
1.119	1.125	-	-	-	-	0.790	0.794	1.408	1.412	2003
1.032	1.038	-	-	-	-	0.733	0.737	1.408	1.412	2004
1.187	1.192	-	-	-	-	0.816	0.820	1.408	1.412	2005
1.072	1.077	-	-	-	-	0.718	0.722	1.408	1.412	2006
0.954	0.959	-	-	-	-	0.704	0.708	1.408	1.412	2007
0.999	1.004	-	-	-	-	0.974	0.979	1.408	1.412	2008
0.979	0.984	-	-	-	-	0.875	0.879	1.408	1.412	2009
1.063	1.068	-	-	-	-	0.907	0.911	1.408	1.412	2010
1.088	1.094	-	-	-	-	0.910	0.915	1.408	1.412	2011
1.066	1.072	-	-	-	-	0.871	0.875	1.408	1.412	2012

(1) : Since January 1, 2002 this currency has been replaced by the Euro.

(2) : Represents ECU during 1993-1998.

(1) : تم استبدال هذه العملة بوحدة اليورو اعتبارا من 2002/1/1.

(2) : تمثل الوحدة الحسابية الاوروبية خلال الفترة 1993- 1998.

Appendix 2

Drugs in this study were selected according to the following inclusion and exclusion criteria:

Inclusion criteria:

- Drug used for chronic medical condition.

Exclusions Criteria:

- If a drug is already available as generic in 1987, as the effect of generic launch on originator price cannot be determined from BNF.
- Controlled drugs (CDS).
- Modified or sustained release preparations.
- Less suitable for prescribing based on UK guidelines in March 2010.
- Parenteral drugs.
- Combination products.
- Brands specific prescribing required based on UK practice e.g., diltiazem and insulin.
- Drugs for acute conditions and drugs for treatment of acute exacerbation of chronic conditions e.g., oral steroids and nebules.
- If an originator was withdrawn before a generic appeared e.g., etodolac.
- Drug that are not prescribed and dispensed in the communit e.g .,HIV drugs.
- If an originator brand couldn't be identified e.g., isosorbide mononitrate.
- Medical devices e.g. peak flow meters.
- Drugs available as British Pharmacopeia formula e.g. aqueous cream.
- Drugs not used for a chronic medical condition e.g., oral contraceptive and drugs for substance dependence.
- Agents used as food for enteral nutrition or foods for special diets.

The following chapters of BNF were completely excluded; infections, immunological products and vaccines and anesthesia used, as the products listed within them are not mainly used for chronic conditions

1. Gastro-Intestinal System

➢ Dyspepsia and gastro-oesophageal reflux disease

• Antacid and simeticone

ALUMINIUM HYDROXIDE	Excluded: Used for Acute condition
MAGNISIUM CARBONATE	Excluded: Used for Acute condition, available as British Pharmacopeia formula
MAGNISIUM TRISILICATE	Excluded: Used for Acute condition available as British Pharmacopeia formula
HYDROTALCITE	Excluded: Used for Acute condition,
ANTACID PREPARATIONS CONTAINING SIMETICONE	Excluded: Used for Acute condition,
SIMETICONE ALONE	Excluded: Used for Acute condition, Less suitable for prescribing based on UK guidelines March 2010

• Compound alginates and proprietary indigestion preparations

ALGINATE RAFT-FORMING ORAL SUSPENSION	Excluded: Used for Acute condition, Combination Product
OTHER COMPOUND ALGINATE PREPARATION	Excluded: Used for Acute condition, Combination Products

➢ Antispasmodics and other drugs altering gut motility (Excluded: Drugs used for acute conditions)

➢ Antisecretory drugs and mucosal protectants

• H_2- receptor antagonist

CIMITEDINE	Included
FAMOTIDINE	Included
NIZATIDINE	Included
RANITIDINE	Included

• Chelates and complexes

TRIPOTASSIUM DICITRATOBISMUTHATE	Included
SUCRALFATE	Included

• Prostaglandin analogues

MISOPROSTOL	Included

- **Proton pump inhibitors**

ESOMEPRAZOLE	Included
LANSOPRAZOLE	Included
OMEPRAZOLE	Included
PANTOPRAZOLE	Included
RABEPRAZOLE	Included

➢ **Acute Diarrhoea** (Excluded: Drugs used for acute conditions)

➢ **Chronic bowel disorder**

- **Aminosalicylates**

BALSALAZIDE SODIUM	included
MESALAZINE	Excluded: Brands specific prescribing
OLSALAZINE SoDIUM	Included
SULFASALAZINE (Sulphasalazine)	Included

- **Corticosteroids**

BECLOMETASONE	Excluded: Used for Acute exacerbation of chronic condition,modified release.
BUDESONIDE	Excluded: Used for Acute exacerbation of chronic condition
HYDROCORTISONE	Excluded: Used for Acute exacerbation of chronic condition
PREDNISOLONE	Excluded: Used for Acute exacerbation of chronic condition.

- **Drugs affecting the immune response**

AZATHIOPORINE	Included
CICLOSPORIN (Cyclosporin)	Excluded: Brands Specific prescribing required based in UK practise.
MERCAPTOPURINE	Included
METHOTREXATE	Excluded: generic was available in BNF 14 (1987),
ADALIMUMAB	Excluded: parenteral drugs
INFLIXIMAB	Excluded: parenteral drugs

- **Food allergy**

SODIUM CROMOGLICATE (Sodium cromoglycate)	Excluded: Used for Acute condition

➢ **Laxative** (Excluded: Drugs used for acute conditions)

➢ **Local preparation for anal and rectal disorders** (Excluded: Drugs used for acute conditions)

➢ **Drug affecting intestinal secretions** (Excluded: Drugs used for acute conditions)

2. Cardiovascular system

➢ **Positive inotropic drugs**

- **Cardiac glycosides**

DIGOXIN	Excluded: generic was available in BNF 14
DIGITOXIN	Excluded: generic was available in BNF 14
DIGOXIN SPECIFIC ANTIBODY	Excluded: Parenteral

- **Phosphodiesterase inhibitors**

ENOXIMONE	Excluded: Parenteral
MILRINONE	Excluded: Parenteral

➢ **Diuretics**

- **Thiazide and related diuretics**

BENDROFLUMETHIAZIDE (Bendrofluazide)	Excluded: generic was available in BNF 14
CHLORTALIDONE	Included
CYCLOPENTHIAZIDE	Included
INDAPAMIDE	Included
METOLAZONE	Included
XIPAMIDE	Included

- **Loop diuretics**

FUROSEMIDE (Frusemide)	Excluded: generic was available in BNF 14
BUMETANIDE	Included
TORASEMIDE	Included

- **Potassium-sparing diuretics and aldosterone antagonists**

AMILORIDE HYDROCHLORIDE	Included
TRIAMTERENE	Included
EPLERENONE	Included

SPIRONLACTONE	Excluded: generic was available in BNF 14
POTASSIUM SPARING DIURETICS WITH OTHER DIURETICS	Excluded: Combination Products

- **Osmotic diuretics**

MANNITOL	Excluded: Parenteral

- **Diuretic with Potassium (Excluded: less suitable for prescribing)**

➢ **Anti-arrhythmic drugs**

ADENOSINE	Excluded: Parenteral
AMIODARONE HYDROCHLORIDE	Included
DISOPYRAMIDE	Excluded: generic was available in BNF 14
FLECAINIDE ACETATE	Included
PROPAFENONE	Included
LIDOCAINE (Ligocaine)	Excluded: Parental preparation

➢ **Beta-adrenoceptor blocking drugs**

PROPRANOLOL	Excluded: generic was available in BNF 14
ACEBUTOLOL	Included
ATENOLOL	Included
BISOPROLOL FUMARATE	Included
CARVEDILOL	Included
CELIPROLOL HYDROCHLORIDE	Included
ESMOLOL	Excluded: Parenteral
LEBATOLOL	Excluded: generic was available in BNF 14
METOPROLOL TARTARATE	Excluded: generic was available in BNF 14
NADALOL	Included
NABIVOLOL	Included
OXPRENOLOL	Excluded: generic was available in BNF 14
PINDOLOL	Included
SOTALOL	Excluded: generic was available in BNF 14
TIMOLOL MALEATE tablet	included

➢ **Hypertension and heart failure**

- **Vasodilator antihypertensive drugs**

AMBRISENTAN	Included
BOSENTAN	Included
DIAZOXIDE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010., parental

HYDRALAZINE HYDROCHLORIDE	Included
ILOPROST	Excluded: Nebulised solution
MINOXIDIL	Included
SLIDENAFIL	Included
SITAXENTAN SODIUM	Included
SODIUM NITROPRUSSIDE	Excluded: Parental preparation

- **Centrally acting antihypertensive drugs**

CLONIDINE HYDROCHLORIDE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010
METHYL DOPA	Excluded: generic was available in BNF 14
MOXONIDINE	Included

- **Adrenergic neurone blocking drugs**

GUANETHIDINE MONOSULPHATE	Excluded: Parental preparation, less suitable for prescribing based on UK guidelines in March 2010

- **Alpha-adrenoceptor blocking drugs**

DOXAZOSIN	Included
INDORAMIN	Included
PRAZOSIN	Included
TERAZOSIN	Included
PHENOXYBENZAMINE HYDROCHLORIDE	Included
PHENTOLAMINE MESILATE	Excluded: Parental

- **Drug affecting the renin-angiotensin system**
  - Angiotensin-converting enzymes inhibitors

CAPTOPRIL	Included
CLIZAPRIL	Included
ENALAPRIL MALEATE	Included
FOSINOPRIL SODIUM	Included
IMIDAPRIL HYDROCHLORIDE	Included
LISINOPRIL	Included
MOEXIPRIL HYDROCHLORIDE	Included
PERINDOPRIL ERBUMINE	Included
QUINAPRIL	Included
RAMIPRIL	Included

TRANDOLAPRIL	Included

- Angitensin-II- Receptor antagonists

CANDESARTAN CILEXTIL	Included
EPROSARTAN	Included
IRBESARTAN	Included
LOZARTAN POTASSIUM	Included
OLMESARTAN MEDOXOMIL	Included
TELMISARTAN	Included
VALSARTAN	Included

- Renin inhibitors

ALISKIREN	Included

➢ **Antianginal drugs**

- **Nitrates**

GLYCERYL TRINITRATE	Excluded: generic was available in BNF14 (1987)
ISOSORBIDE DINITRATE	Excluded: originator brand couldn't be identified.
ISOSORBIDE MONONITRATE	Excluded: originator brand couldn't be identified.

- **Calcium-channel blockers**

AMLODIPINE	Included
DILTIAZIM	Excluded: Brands specific prescribing required based on UK practice
FELODIPINE	Excluded: modified release
ISRADIPINE	Included
LACIDIPINE	Included
LERCANIDIPINE	Included
NICRADIPINE	Included
NIFIDIPINE	Included
NIMODIPINE	Included
VERAPAMIL HYDROCHLORIDE	Excluded: generic was available in BNF14 (1987)

- **Other antianginal drugs**

IVABRADINE	Included
NICORANDIL	Included
RANOLAZINE	Excluded: modified release

- **Peripheral vasodilators and related drugs**

CILOSTAZOL	Included
INOSITOL NICOTINATE	Excluded: less suitable for prescribing based on UK guidelines in March 2010
MOXISYLYTE (Thymoxamine)	Excluded: less suitable for prescribing based on UK guidelines in March 2010
NAFTIDROFURYL OXALATE	Included
PENTOXIFYLLINE (Oxpentifylline)	Excluded: less suitable for prescribing based on UK guidelines in March 2010, modified release

➢ Sympathomimetics

- **Inotropic sympathomimetics**

DOBUTAMINE	Excluded: Parenteral
DOPAMINE HYDROCHLORIDE	Excluded: Parenteral
DOPEXAMINE HYDROCHLORIDE	Excluded: Parenteral

- **Vasoconstrictor sympathomimetics**

EPHYDRINE HYDROCHLORIDE	Excluded: Parenteral
METARAMINOL	Excluded: Parenteral
NORADRENALINE ACID TARTRATE (NOREPINEPHRINE BITARTRATE)	Excluded: Parenteral
PHENYLEPHRINE HYDROCHLORIDE	Excluded: Parenteral

- **Cardiopulmonary resuscitation**

ADRENALINE/EPINEPHRINE	Excluded: Parenteral

➢ Anticoagulant and Protamine

- **Parenteral anticoagulant (Excluded: parenteral preparations)**

- **Oral anticoagulant**

WARFARIN SODIUM	Excluded: generic was available in BNF 14 (1987)
ACENOCOUMAROL (Nicoumalone)	Included
PHENINDIONE	Excluded: originator was withdrawn before generic launch
DABIGATRIN ETEXALATE	Included
RIVAROXABAN	Included

- **Protamine Sulphate**

PROTAMINE SULPHATE (protamine sulphate)	Excluded: Parenteral

➢ **Antiplatelet drugs**

ABCIXIMB	Excluded: Parenteral
ASPIRIN (Acetylsalysalic Acid)	Excluded: generic was available in BNF 14 (1987)
CLOPIDOGREL	Included
DIPYRIDAMOLE	Included
EPITIFIBATIDE	Excluded: Parenteral
PRASUGREL	Included
TIROFIBAN	Excluded: Parenteral

➢ **Myocardial infarction and fibrinolysis**

- **Fibrinolytic drugs**

ALTEPLASE	Excluded: Parenteral
RETEPLASE	Excluded: Parenteral
STREPTOKINASE	Excluded: Parenteral
TENECTEPLASE	Excluded: Parenteral
UROKINASE	Excluded: Parenteral

➢ **Antifibrinolytic drugs**

ETAMSYLATE (Ethamsylate)	Included
TRANEXAMIC ACID	Included

➢ **Lipid regulating drugs**

ATORVASTATIN	Included
FLUVASTATIN	Included
PRAVASTATIN SODIUM	Included
ROSUYASTATIN	Included
SIMVASTATIN	Included
COLESEVELAM HYDROCHLORIDE	Included
COLESTYRAMINE (Cholestyramine)	Included
COLESTIPOL HYDROCHLORIDE	Included
EZETIMIBE	Included
BIZAFIBRATE	Included
CIPROFIBRATE	Included
FENOFIBRATE	Included
GEMFIBROZIL	Included
ACIPIMOX	Included

NICOTINIC ACID	Excluded: modified release or Combination product
OMEGA-3-ACID ETHYL ESTERS	Excluded: Combination product
OMEGA-3-MARINE TRIGLYCERIDE	Excluded: Combination product

➢ **Local sclerosants**

ETHANOLAMINE OLEATE	Excluded: Parenteral
SODIM TETRADECYL SULPHATE	Excluded: Parenteral

3. Respiratory system

➢ **Bronchodilators**

- **Adrenoceptor agonists**

  - Selective beta$_2$ agonists

BAMBUTEROL HYDROCHLORIDE	Included
FENOTEROL HYDROCHLORIDE	Excluded: Combination Products, drugs for acute exacerbation of chronic condition (Nebuliser)
FORMETROL FUMARATE (Efomoterol fumarate): -Foradil -Atimos Modulate -Oxis Turbohaler	 Included Included included
Salbutamol (Albuterol) -oral: tablet & syrup -injection -inhalation: --Aerosol inhalation --Rota Caps --Nebules	 Excluded: generic was available in BNF 14 Excluded: Parenteral preparation Excluded: generic was available in BNF 14 Included Excluded: drugs for Acuteexacerbation of chronic condition
SALMETROL -Accuhaler -Evohaler -Diskhaler	 Included Included Included
TERBUTALINE SULPHATE -tablet -injection Inhalation: ■ Turbohaler (dry powder inhaler) ■ Respules (Nebulisation dose unit)	 Excluded: generic was available in BNF 14 Excluded: Parenteral Preparation Included Excluded: drugs for Acuteexacerbation of

	chronic condition

- Other adrenoceptor agonists

EPHEDRINE HYDROCHLORIDE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010, generic was available in BNF 14 (1987)
ORCIPRENALINE SULPHATE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010

- **Antimuscarinic bronchodilators**

IPRATROPIUM BROMIDE - Aerosol inhalation - Nebuliser solution - Aerohaler	 included Excluded: for acute exacerbation of chronic condition. Included
TIOTROPIUM - Inhalation powder - Solution for inhalation	 Included included

- **Theophylline**

THEOPHYLINE	Excluded: Modified release preparations
AMINOPHYLLINE	Excluded: generic was available in BNF 14 (1987) ,Modified release, parenteral preparation also available

➢ **Corticosteroids**

BECLOMETASONE DIPROPIONATE (Beclomethasone Dipropionate) - Aerosol inhalation - Suspension for nebulisation - Dry powder for inhalation - Autohaler (breath actuated aerosol inhalation)	 Included Excluded: for acute exacerbation of chronic condition Included included
BUDESONIDE Dry powder for inhalation - Aerosol inhalation	 Included included
CICLESONIDE - Aerosol inhalation	 included
FLUTICASONE PROPIONATE - Accuhaler (dry powder for inhalation) - Diskhaler (dry powder for inhalation) - Evohaler (aerosol inhalation) - Nebules - Compound product	 Included Included Included Excluded: for acute exacerbation of chronic condition

	Excluded: compound product
MOMETASONE FUROATE(Twisthaler dry powder inhaler)	Included

- **Cromoglicate and related therapy and leukotriene receptor antagonists**

  - **Cromoglicate and related therapy**

SODIUM CROMOGLICATE (Sodium Cromoglycate) Aerosol inhalation	Included
NEDOCRAMIL SODIUM Aerosol inhalation	Included

  - **Leukotriene receptor antagonists**

MONTELUKAST -Chewable tabet -granules	 Included included
ZAFIRLUKAST –tablet	Included

Excluded: for acute exacerbation of chronic condition

- **Antihistamines and hyposesitisation, and allergic emergencies** (Excluded: Drugs for acute conditions)

- Respiratory Stimulants and pulmonary Surfactants

  - **Respiratory Stimulants** (Excluded: not chronic medical conditions)
  - **Pulmonary Surfactants** (Excluded: Drugs used for acute conditions, drugs used for diseases not treated (dispensed) by community practitioner)

- **Mucolytics** (Excluded: Drugs used for acute conditions, drugs for treatment of acute exacerbation of chronic conditions)
- **Aromatic Inhalation** (Excluded: Drugs for acute conditions)
- **Cough Preparation** (Excluded: Drugs for acute conditions)
- **Systemic Nasal Decongestants** (Excluded: Less suitable for prescribing based on UK guidelines in March 2010)

4. Central Nervous System

- **Hypnoyics and anxiolytics** (Excluded: Drugs for acute conditions)

- **Drugs used in psychoses and related disorders**

  - **Antipsychotic Drugs**

BENPERIDOL	Included
CHLORPROMAZINE HYDROCHLORIDE	Excluded: generic was available in BNF 14

	(1987)
FLUPENTIXOL (Flupenthixol)	Included
HALOPERIDOL	Included
LEVOMEPROMAZINE (Methotrimeprazine)	Included
PERICYAZINE (Periciazine)	Included
PERPHENAZINE	Included
PIMOZIDE	Included
PROCHLORPERAZINE	Included
PROMAZINE HYDROCHLORIDE	Excluded: Originator was withdrawn before generics appeared.
SULPIRIDE	Excluded: generic was available in BNF 14 (1987)
TRIFLUOPERAZINE	Included
ZUCLOPENTHIXOL ACETATE	Excluded: Parenteral
ZUCLOPENTHIXOL	Included
AMISULPRIDE	Included
ARIPIPRAZOLE	Included
CLOZAPINE	Included
OLANZAPINE	Included
PALIPERIDONE	Excluded: Modified Release
QUETIAPINE	Included
RISPERIDONE	Included
SERTINDOLE	Excluded: price not available in BNFs
ZOTEPINE	Included

- **Antipsychotic depot injections (Excluded: Parenteral preparations**

- **Antimanic drugs**

VALPROIC ACID	Included
LITHIUM CARBONATE	Excluded: Modified release, Brands specific prescribing required based on UK practice
LITHIUM CITRATE	Excluded: Modified release, Brands specific prescribing required based on UK practice

➢ **Antidepressant drugs**

- **Tricyclic and related antidepressant drugs**

AMITRIPTYLINE HCL	Excluded: Generic was available in BNF 14 (1987)
CLOIPRAMINE HCL	Included
DOSULEPIN	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.
DOXEPIN	Included
IMIPRAMINE HCL	Excluded: Generic was available in BNF 14 (1987)
LOFEPRAMINE	Included
NORTRIPTYLINE	Included
TRIMIPRAMINE	Included

MIANSERIN	Included
TRAZODONE	Included

- **Monoamine-oxidase inhibitors**

PHENELZZINE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.
ISOCARBOXAZID	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.
TRANYLCYPROMINE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.
MOCLOBEMIDE	Included

- **Selective serotonin re-uptake inhibitors**

CITALOPRAM	Included
ESCITALOPRAM	Included
FLUOXETINE	Included
FLUVOXAMINE MALEATE	Included
PAROXETINE	Included
SERTRALINE	Included

- **Other antidepressant drugs**

AGOMELATINE	Included
DULOXETINE	Included
FLUPENTIXOL (Flupenthixol)	Included
MIRTAZAPINE	Excluded: Originator was withdrawn before generic appeared
REBOXETINE	Included
TRYPTOPHAN	Included
VENLAFAXINE	Included

➢ **CNS stimulants and drugs used for attention deficit hyperactivity disorder**

ATOMOXETINE	Included
DEXAMFETAMINE SULPHATE	Included
METHYLPHENIDATE HYDROCHLORIDE	Excluded: Controlled Drugs (CDs)
MODAFINIL	Included

➢ **Drugs used in the treatment of obesity**

- **Anti-obesity drugs acting on the gastro-intestinal tract**

ORLISTAT	Included

- **Centrally acting appetite suppressants**

SIBUTRAMINE HYDROCHLORIDE	Included

➢ **Drugs used in nausea and vertigo** (Excluded: Drugs used for acute conditions)

➢ **Analgesics**

- **Non-opioid analgesics** (Excluded: Drugs used for acute conditions)
- **Opioid analgesics** (Excluded: Controlled drugs (CDs), drugs used for acute conditions)
- **Treatment of acute migraine** (Excluded: Drugs used for acute conditions)
- **Prophylaxis of migraine**

PIZOTIFEN	Included
CLONIDINE HYDROCHLORIDE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.
METHYSERGIDE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010.

➢ **Antiepileptic drugs**

- **Control of epilepsy**

CARBAMAZIPINE	Excluded: Generic was available in BNF 14 (1987)
ESLICARBAZEPINE ACETATE	Included
OXCARBAZEPINE	Included
ETHOSUXIMIDE	Excluded: Originator was withdrawn before generic appeared
GABAPENTIN	Included
PREGABLIN	Included
LACOSAMIDE	Included
LAMOTRIGINE	Included
LEVETIRACTEM	Included
PHENOBARBITAL	Excluded: Generic was available in bnf 14 (1987),Controlled Drugs (CDs)
PRIMIDONE	Included
PHENYTOIN	Excluded: generic was available in BNF 14, on the basis of single dose tests there are no clinically relevant differences in bioavailability between available phenytoin sodium tablets and capsules but there may be pharmacokinetics basic for maintain the same brand of phenytoin in some patients originator capsules and generic tablets (different dosage forms)
RUFINAMIDE	Included
TIAGABINE	Included
TOPIRAMATE	Included
SODIUM VALPROATE	Included
VIGABATRIN	Included
ZONISAMIDE	Included
CLOBAZAM	Excluded: Drug for acute conditions

CLONAZEPAM	Excluded: Drug for acute conditions

- **Drug used in status epilepticus** (Excluded: Drugs used for acute conditions)

➢ **Drug used in parkinsonism and related disorders**

- **Dopaminergic drugs used in parkinsonism**

APOMORPHINE HCL	Excluded: Parenteral
BROMOCRIPTINE	Included
CABERGOLINE	Included
PERGOLIDE	Included
PARAMIPEXOLE	Included
ROPINIROLE	Included
ROTIGITONE	Included
CO-BENELDOPA	Excluded: Combination products
CO-CARELDOPA	Excluded: Combination products
RASAGLINE	Included
SELEGLINE HCL	Included
ENTACAPONE	Included
TOLCAPONE	Included
AMANTADINE HCL	Included

- **Antimuscarinic drugs used in parkinsonism**

ORPHENADRINE HCL	Included
PROCYCLIDINE HCL	Included
TRIHEXPHENIDYL HYDROCHLORIDE (Bezhexol hydrochloride)	Excluded: generic was available in BNF 14 (1987)

- **Drugs used in essential tremor, chorea, tics, and related disorder**

HALOPERIDOL	Included
PIRECETAM	Included
RILUZOLE	Included
TETRABENAZINE	Included
BOTULINUM TOXIN TYPE A	Excluded: Parenteral, Brand specific
BOTULINUM TOXIN TYPE B	Excluded: Parenteral, Brand specific

➢ **Drugs used in substance dependence** (Excluded: Drugs for not chronic condition or prevention medication not used for a chronic medical conditions)

➢ **Drugs for dementia**

DONEPEZIL HYDROCHLORIDE	Included
GALANTAMINE	Included
MEMANTINE HYDROCHLORIDE	Included
RIVASTIGMINE	Included

5. Infection

All drugs in chapter 5 excluded since they are for acute conditions.

6. Endocrine systems

➢ Drug used in diabetes

- **Insulin** (Excluded: Brands specific prescribing required based on UK practice)

- **Antidiabetic drugs**
  - Sulphonnylureas

GLIBENCLAMIDE	Excluded: generic was available in BNF 14 (1987)
GLICLAZIDE	Included
GLIMEPRIDE	Included
GLIPIZIDE	Excluded: generic was available in BNF 14 (1987)
TOLBUTAMIDE	Excluded: generic was available in BNF 14 (1987)

  - Biguanides

METFORMIN HYDROCHLORIDE	Excluded: generic was available in BNF 14 (1987)

  - Other antidiabetic drugs

ACARBOSE	Included
EXENATIDE	Excluded: Parenteral
LIRAGLUTIDE	Excluded: Parenteral
NATEGLINIDE	Included
PIOGLITAZONE	Included
REPAGLINIDE	Included
ROSIGLITAZONE	Included
SAXAGLIPTIN	Included
SITAGLIPTEN	Included
VILDAGLIPTINE	Included

- **Treatment of hypoglycaemia**

GLUCAGON	Excluded: Parenteral
DIAZOXIDE	Included

➢ Thyroid and antithyroid drugs

- **Thyroids hormone**

LEVOTHYROXINE SODIUM (Thyroxine sodium)	Excluded: generic was available in BNF 14 (1987)
LIOTHYRONINE SODIUM	Excluded: generic was available in BNF 14 (1987)

- **Antithyroid drugs**

CARBIMAZOLE	Included
IODINE AND IODIDE	Excluded: available as British pharmacopeia formula
PROPYLTHIOURACIL	Excluded: generic was available in BNF 14 (1987)

➢ **Corticosteroids** (Excluded: Drugs used for treatment of acute exacerbation of chronic conditions)

➢ **Sex hormones** (Excluded: Drugs used for short period only, committee on safety of medicine)

➢ **Hypothalamic and pituitary hormones and anti-oestrogens**

- **Hypothalamic and anterior pituitary hormones** (Excluded: Short Term)

- **Growth hormone receptor antagonists**

PEGVISOMANT	Excluded: Parenteral

- **Posterior pituitary hormones and antagonists** (Excluded: Drugs used for acute conditions)

➢ **Drugs Effecting Bone Metabolism**

- **Calcitonin and parathyroid hormones**

CALCITONIN (SALMON)/ SALCATONIN	Included
PARATHYROID HORMONE	Excluded: Parenteral
TERIPARATIDE	Excluded: Parenteral

- **Bisphosphonates and other drugs affecting bone metabolism**

ALENDRONIC ACID	Included
DISODIUM ETIDRONATE	Included
DISODIUM PAMIDRONATE	Excluded: Parenteral
IBRANDRONIC ACID	Included
RESIDRONATE SODIUM	Included
SODIUM CLODRONATE	Included
TILUDRONIC ACID	Included
ZOLEDRONIC ACID	Excluded: Parenteral
STRONTIM RANELATE	Included

➢ **Other endocrine drugs**

- **Bromocriptine and other dopaminergic drugs**

BROMOCRIPTINE	Included
CABERGOLINE	Included
QUINAGOLIDE	Included

- **Drugs affecting gonadotrophins** (Excluded: Drugs used for acute conditions)

7. Obstetrics, gynaecology, and urinary-tract disorders

➢ **Drugs used in obstetrics** (Excluded: Drugs not used for a chronic medical conditions)

➢ **Treatment of vaginal and vulval conditions** (Excluded: Drugs used for acute conditions, drugs not used for a chronic medical conditions)

➢ **Contraceptives** (Excluded: Drugs not used for a chronic medical conditions)

➢ **Drugs for genitor-urinary disorders**

- **Drugs for urinary retention**

ALFUZOSIN HYDROCHLORIDE	Included
DOXAZOSIN	Included
INDORAMIN	Included
PRAZOSIN	Included
TAMSULOSIN HYDROCHLORIDE	Excluded: Modified Release
TERAZOSIN	Included
BETHANECHOL CHLORIDE	Excluded: less suitable for prescribing based on UK guidelines in March 2010
DISTIGMINE BROMIDE	Included

- **Drugs for urinary frequency, enuresis, and incontinence**

DIARIFENACIN	Excluded: Modified Release
DULOXETINE	Included
FESOTERODINE FUMARATE	Excluded: Modified Release
FLAVOXATE HYDROCHLORIDE	Included
OXYBUTYNIN HYDROCHLORIDE	Included
PROPANTHELINE BROMIDE	Included
PROPIVERINE HYDROCHLORIDE	Included
SOLIFENACIN SUCCINATE	Included
TOLTERODINE TARTARATE	Included
TROSPIUM CHLORIDE	Included

- **Drugs used in urological pain** (Excluded: Drugs used for acute conditions)
- **Drugs for** erectile dysfunction (Excluded: Drugs not used for a chronic medical condition)

8. Malignant disease and immunosuppression

➢ Cytotoxic drugs (Excluded: Drugs used for conditions not treated or dispensed in community, and mostly parenteral)

➢ **Drugs affecting the immune response**

- **Antiproliferative immune suppressants:**

AZATHIOPRINE	Excluded: generic was available in BNF 14 (1987)
MYCOPHENOLATE MOFETIL	Included

- **Corticosteroids and other immunosuppressants** (Excluded: short term use, drugs used for acute exacerbation of chronic conditions)

- **Rituximab and alemtuzumab**

ALEMTUZUMAB	Excluded: Parenteral
RITUXIMAB	Excluded: Parenteral

- **Other immunomodulating drugs**

INTERFERON ALFA	Excluded: Parenteral
PEGINTERFERON ALFA	Excluded: Parenteral
INTERFERON BETA	Excluded: Parenteral
INTERFERON GAMMA	Excluded: Parenteral
ALDESLEUKIN	Excluded: Parenteral
BACILLUS CALMETTE GUERN	Excluded: Parenteral
GLATIRMARE ACETATE	Excluded: Parenteral
LENALIDOMIDE	Included
THALIDOMIDE	Included
NATALIZUMAB	Excluded: Parenteral

➢ **Sex hormones and hormone antagonists in malignant disease**

- **Oestrogens**

DIETHYLSTILBESTROL (Stilboesterol)	Excluded: Generic was available in BNF 14 (1987)
ETHINYLSTRADIOL (Ethinyloestradiol)	Excluded: Generic was available in BNF 14 (1987)

- **Progestogens**

MEDROXYPROGESTERONE ACETATE	Included
MEGESTROL ACETATE	Included
NORETHISTERONE	Excluded: Generic was available in BNF 14 (1987)

- **Hormone Antagonists**

  - Breast Cancer

ANASTROZOLE	Included
EXEMESTANE	Included
FULVAESTRANT	Excluded: Parenteral
LETROZOLE	Included
TAMOXIFEN	Excluded: generic was available in BNF 14 (1987)
TOREMIFEN	Included

  - Gonadorelin analogues and gonadotrophin - releasing hormone antagonists

BUSERELIN	Excluded: Parenteral
GOSERELIN	Excluded: Parenteral
HISTRELIN	Excluded: Parenteral
LEUPRORELIN ACETATE	Excluded: Parenteral
TRIPTORELIN	Excluded: Parenteral
DEGARELIX	Excluded: Parenteral
BICLUTAMIDE	Included
CYPROTERONE ACETATE	Included
FLUTAMIDE	Included

  - Somatostatin analogues (Excluded: Parenteral preparations)

9. Nutrition and Blood

➢ Anaemias and some other blood disorders

- **Iron-deficiency anaemia**

  - Oral iron (Excluded: drugs for short term use)
  - Parenteral iron (Excluded: Parenteral preparations)

- **Drugs used in megaloblastic anaemias** (Excluded: drugs for short term use)

- **Drugs used in hypoplastic, haemolytic, and renal anaemias**

  - Erythropoietins

DARBEPOETIN ALFA	Excluded: Parenteral
EPOTEN ALFA, BETA and ZETA	Excluded: Parenteral
METHOXY POLYETHYLENE GLYCOL EPOTIN BETA	Excluded: Parenteral

  - Sickle-cell disease

HYDROXYCARBAMIDE	Included

  - Iron overload

DEFRASIROX	Included
DEFRIPRONE	Included
DESFERRIOXAMINE MESILATE	Excluded: Parenteral

  - Paroxysmal nocturnal haemoglobinuria

ECULIZUMAB	Excluded: Parenteral

- **Drugs used in platelet disorders** (Excluded: Drugs used for short term, not dispensed in the community)
- **Drugs used in neutropenia** (Excluded: Drugs for acute conditions, parenteral preparations)
- **Drugs used to mobilise stem cell** (Excluded: Drugs used for acute conditions, parenteral preparations)

➢ **Fluids and electrolytes** (Excluded: Drugs used for acute conditions, short term replacement)

➢ **Intravenous nutrition** (Excluded: Parenteral preparations, agents used as food or for enteral nutrition or foods for special diets)

➢ **Oral Nutrition** (Excluded: Agents used as food or for enteral nutrition or foods for special diets)

➢ **Minerals** (Excluded: Short term replacement)

➢ **Vitamins** (Excluded: Drugs used for acute conditions)

➢ **Metabolic disorders**

- **Drugs used in metabolic disorders**

  - Wilson's disease

PENICILLAMINE	Excluded: generic was available in BNF 14 (1987)
TRIENTINE DIHYDROCHLORIDE	Excluded: no price data available
ZINC ACETATE	Included

- Carnitine deficiency

CARNITINE	Included

- Fabry's disease

AGALSIDASE ALFA and BETA	Excluded: Parenteral

- Gaucher's disease

IMIGLUCERASE	Excluded: Parenteral

- Mucopolysaccharidosis

GALSULFASE	Excluded: Parenteral
IDURSULFASE	Excluded: Parenteral
LARONIDASE	Excluded: Parenteral

- Nephropathic cystamine

MERCAPTAMINE (Cysteamine)	Included

- Pompe disease

ALGLUCOSIDASE ALFA	Excluded: Parenteral

- Tyrosinaemia type I

NITISINONE (NTBC)	Included

- Urea cycle disorders

CARGLUMIC ACID	Included
SODIUM PHENYLBUTYRATE	Included

- Homocystinuria

BETAINE	Included

- Other metabolic disorder

MIGLUSTAT	Included

- **Acute porphyrias** (Excluded: Drugs used for acute conditions, not long term)

10. Musculoskeletal and joint diseases

➢ Drugs used in rheumatic diseases and gout

- **Non-steroidal anti-inflammatory drugs**

ACECLOFENAC	Included
ACEMTACIN	Included
AZAPROPAZONE	Excluded: Less suitable to prescribing based on UK guidelines in March 2010
CELECOXIB	Included
DEXIBUPROFEN	Included
DEXKETOPROFEN	Included
DICLOFENAK SODIUM	Excluded: generic was available in BNF 14 (1987)
ETODOLAC	Excluded: originator was withdrawn before a generic appeared
ETORICOXIB	Included
FENBUFEN	Included
FENOPROFEN	Included
FLURBIPROFEN	Included
IBUPROFEN	Excluded: generic was available in BNF 14 (1987)
INDOMETACIN (Indomethacin)	Excluded: generic was available in BNF 14 (1987)
KETOPROFEN	Excluded: generic was available in BNF 14 (1987)
MEFENAMIC ACID	Excluded: generic was available in BNF 14 (1987)
MELOXICAM	Included
NABUMETONE	Included
NAPROXIN	Excluded: generic was available in BNF 14 (1987)
PIROXICAM	Excluded: Less suitable for prescribing based on UK guidelines in March 2010, generic was available in BNF 14 (1987)
SULINDAC	Included
TENOXICAM	Included
TIAPROFENIC ACID	Included

- **Corticosteroids** (Excluded: Drugs used for acute exacerbation of chronic conditions)

- **Drugs that suppress the rheumatic diseases process**

SODIUM AUROTHIOMALATE	Excluded: Parenteral
PENICILLAMINE	Excluded: generic was available in BNF 14 (1987)
CHLOROQUINE	Excluded: generic was available in BNF 14 (1987)

HYDROXYCHLOROQUINE SULPHATE	Included
AZATHIOPRINE	Excluded: generic was available in BNF 14 (1987)
CICLOSPORIN	Excluded: Because of different bioavailability brand should be specified by prescriber
LEFLUNOMIDE	Included
METHOTREXATE	Excluded: generic was available in BNF 14 (1987)
ABATACEPT	Excluded: Parenteral
ADALIMUMAB	Excluded: Parenteral
ANAKINRA	Excluded: Parenteral
CERTOLIZUMAB PEGOL	Excluded: Parenteral
ETANERCEPT	Excluded: Parenteral
INFLIXIMAB	Excluded: Parenteral
RITUXIMAB	Excluded: Parenteral
TOCLIZUMAB	Excluded: Parenteral
SULFASALAZINE (Sulphasalazine)	Included

- **Acute attack of gout** (Excluded: Drugs used for acute conditions)

- **Long term control of gout**

ALLOPURINOL	Excluded: generic was available in BNF 14 (1987)
PROBENCID	Excluded: originator was withdrawn before a generic appeared
SULFINPYRAZINE (Sulphinpyrazone)	Included

- **Hyperuricemia associated with cytotoxic drugs** (Excluded: Drugs used for acute conditions)

- **Other Drugs for Rheumatic Diseases**

GLUCOSAMINE	Excluded: Less suitable for prescribing based on UK guidelines in March 2010

➢ Drugs used in neuromuscular disorders

- **Drugs that enhance neuromuscular transmission**

NEOSTIGMINE	Excluded: originator was withdrawn before a generic appeared
DISTIGMINE BROMIDE	Included
EDROPHONIUM CHLORIDE	Excluded: Parenteral
PYRIDOSTIGMINE BROMIDE	Included

- **Skeletal muscle relaxants**

BACLOFEN	Included
DANTROLENE SODIUM	Included

DIAZEPAM	Excluded: generic was available in BNF 14 (1987)
TIZANDINE	Included
METHOCARBAMOL	Excluded: Less suitable for prescribing based on UK guidelines in March 2010

- **Nocturnal leg cramps** (Excluded: Drugs used for acute conditions)

➢ Drugs for the relief soft-tissue inflammation

- **Enzymes**

HYALURONIDASE	Excluded: parenteral

- **Rubefacients And Other Topical Antirheumatics**

IBUPROFEN	Excluded: generic was available in BNF 14 (1987)
KETOPROFEN	Excluded: generic was available in BNF 14 (1987)
PIROXICAM	Excluded: generic was available in BNF 14 (1987)
CAPSACIN	Included
POULTICES	Excluded: Less suitable for prescribing based on UK guidelines in March 2010

11. Eye

➢ **Anti-infective eye preparations** (Excluded: Drugs used for acute conditions)

➢ **Corticosteroids and other anti-inflammatory preparations** (Excluded: Drugs used for acute conditions)

➢ **Mydriatics and cycloplegics** (Excluded: Short term use)

➢ **Treatment of glaucoma**

Betaxolol HCL	Included
CARTEOLOL	Included
LEVOBUNOLOL HYDROCHLORIDE	Included
METIPRANOLO	Included
TIMOLOL MALEATE	Included
BIMATOPROST	Included
LATANOPROST	Included
TAFLUPROST	Included
TRAVOPROST	Included
BRIMONIDINE TARTARATE	Included
DIPIVEFRINE HCL	Included
ACETAZOLAMIDE	Included
BRINZOLAMIDE	Included

DORZOLAMIDE	Included
PILOCARPINE	Excluded: generic was available in BNF 14 (1987)

- **Local anaesthetics** (Excluded: Drugs used for acute conditions)
- **Miscellaneous ophthalmic preparations**
  - **Tear deficiency, ocular lubricants, and astringents** (Excluded: Drugs used for acute conditions)
  - **Ocular diagnostic and perioperative preparations and photodynamic treatment** (Excluded: Short term use, diagnostic use only)

12. Ear, nose, and oropharynx

All drugs are excluded short term.

13. Skin

- **Emollient and barrier preparations** (Excluded: Drugs available as British pharmacopeia formula, used for acute conditions)
- **Topical local anaesthetics and antipruritics** (Excluded: Drugs used for acute conditions)
- **Topical corticosteroids** (Excluded: Drugs used for acute conditions and acute exacerbation of chronic conditions)
- **Preparations for eczema and psoriasis**
  - **Preparations for eczema**

ICHTAMMOL	Excluded: Drugs available as British pharmacopeia formula
ALITRETINOIN	Excluded: Drug used for diseases not treated (dispensed) by community practitioner

  - **Preparations for psoriasis**

CALCIPOTRIOL	Included
CALCITRIOL(1,25Dihydroxycholecalciferol)	Included
TACALCITOL	Included
TAZAROTENE	Included
TARS	Excluded: Drugs available as British pharmacopeia formula, used for Acute psoriasis, generic was available in BNF 14 (1987)
DITHRANOL (Anthralin)	Excluded: Drugs available as British pharmacopeia formula, generic was available in BNF 14 (1987)
SALICYLIC ACID	Excluded: Drugs available as British

	pharmacopeia formula, generic was available in BNF 14 (1987),
ACITRETIN	Excluded: Drug used for diseases not treated (dispensed) by community practitioner

- **Drugs affecting the immune response**

AZATHIOPRINE	Excluded: generic was available in BNF 14 (1987)
CICLOSPORIN	Excluded: brand specific prescription, short term treatment maximum 8 weeks
METHOTREXATE	Excluded: generic was available in BNF 14 (1987)
PIMECROLIMUS	Included
TACROLIMUS	Included
ADALIMUMAB	Excluded: Parenteral
ETANERCEPT	Excluded: Parenteral
INFLIXIMAB	Excluded: Parenteral
USTEKINUMAB	Excluded: Parenteral

- **Acne and rosacea** (Excluded: Drugs used for acute conditions)
- **Preparations for warts and calluses** (Excluded: Drugs used for acute conditions)
- **Sunscreens and camouflagers** (Excluded: Drug used for not chronic medical conditions)
- **Shampoos and other preparations for scalp hair conditions** (Excluded: Drugs used for acute conditions)
- **Anti-infective skin preparations** (Excluded: Drugs used for acute conditions)
- **Skin cleansers and antiseptics** (Excluded: Drugs used for not chronic medical conditions, acute conditions)
- **Antiperspirants** (Excluded: Drugs used for not chronic medical conditions, acute conditions)
- **Topical circulatory preparations** (Excluded: Less suitable for prescribing based on UK guidelines March 2010)

14. Immunological products and vaccines

All drugs are excluded since they are for short term use.

15. Anaesthesia

All drugs excluded since they are used for short term (pre-operatives).

Appendix 3

Kingston University London

Participant Information sheet

A cost evaluation analysis to identify solutions for affordable medicines in Jordan - a comparative study with the UK

1st July 2012

You are being invited to take part in a PhD research project. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information sheet carefully before deciding whether or not to participate. If you decide to take part you will have to sign in the box at the end. If after reading this information sheet, you are still unsure or uncertain about anything, then I am happy to answer any questions you may have, so please contact me on the details provided at the end. You should not sign the consent form until your queries have been resolved and you are happy to volunteer.

What is the purpose of the study?

The purpose of the study is to interview stakeholders who are involved in pricing of medicines in Jordan as well as pricing policy and in order to obtain their opinions regarding the prices of medicine and the factors that may influence the pricing of medicines in Jordan in comparison to the United Kingdom.

Why have I been chosen?

As a stakeholder involved in the pricing of medicines in Jordan, your opinion will be of a significant value in the study.

Do I have to take part?

No. This research study is done purely on a voluntary basis. If you do take part, you are still free to withdraw from the study at any point without any disadvantage and without having to provide a reason for the withdrawal.

What will happen to me if I take part?

Firstly you will have to sign the consent form, implying that you are ready to take part in the study then you'll be asked to take part in an interview, which will take around 30-40 minutes. It will be audio taped after your permission.

What are the possible benefits of taking part?

As a stakeholder involved in the pricing of medicine, your contribution and opinion will be of a significant value to draw conclusions and recommendations in my research project in regards to factors that may influence prices of medicines and pricing policy in Jordan.

What are the possible disadvantages and risks of taking part?

There are no disadvantages neither risks of taking part in this interview.

What happens when the research study ends?

You will be under no obligation to volunteer again. Contact details for myself plus project supervisors are included at the end of this information sheet should you wish to ***discuss the findings***.

Will my taking part be kept confidential?

All information collected during the course of the study will be kept strictly confidential and in secure storage. Responses will be anonymised before analysis so that it will not be possible to identify you or any other participant. Only I and the project supervisor will have access to this dataset.
Any personal information collected will be immediately destroyed, except that required by the University research policy.

Who is organising and funding the study?

This study is part of my research of Doctor of Philosophy (PhD) degree, within the School of Pharmacy, Faculty of Science, Engineering and Computing at Kingston University. None of the investigators stand to gain financially from this study.

What will happen to the results of the research study?

The results will be part of my project which will be made available in the Faculty of Science Learning Resources Centre (library) at Kingston University for others to view. In addition, findings arising from this study may be presented at national and international conferences as well as published in scientific journals. It will not be possible to identify you or others from any such publications with results being aggregated for the whole group.
Please contact me or my supervisor on the details provided below, if you have any questions about this project.

Who has reviewed the study?

The Kingston University Faculty of Science Research Ethics Committee has reviewed and approved this study.

Further information may be obtained from:
Faris El-Dahiyat (PhD Candidate) (k0740390@kingston.ac.uk),
Dr.Reem Kayyali (Director of study) (r.kayyali@kingston.ac.uk

Thank you for taking the time to read this information sheet.

Kingston University London

Consent Form

By signing this consent form, you are not waiving your legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

I have read the information presented in the information letter about a study namely "An investigation of the factors that influence the pricing of medicines in Jordan in comparison to the United Kingdom." being conducted by Faris El-Dahiyat from Kingston University. I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted.

I am aware that I have the option of allowing my interview to be audio recorded to ensure an accurate recording of my responses.

I am also aware that excerpts from the interview may be included in the thesis and/or publications to come from this research, with the understanding that the quotations will be anonymous.

I was informed that I may withdraw my consent at any time without penalty by advising the researcher.

This project has been reviewed by, and received ethics clearance through, Ethics Committee at Kingston University.

With full knowledge of all foregoing, I agree, of my own free will, to participate in this study.

☐YES ☐NO

I agree to have my interview audio recorded.

☐YES ☐NO

I agree to the use of anonymous quotations in any thesis or publication that comes of this research.

☐YES ☐NO

Participant Name: _____ (Please print)

Participant Signature: _____

Date: _____

Appendix 4

Interview Schedule for Generic manufacturer

Opening:

Introduce myself and give a brief about my PhD research

Body:

- From a pharmaceutical generic manufacturer point of view, does the current pricing policy live up to your expectations and why?

- [Prompts] in terms of fairness?

- From a pharmaceutical company point of view, is Saudi Arabia a suitable choice as a reference country? And why?

- Which factors does a pharmaceutical manufacturer take into account when applying to JFDA for pricing of a drug?

- According to the statistical analysis of some of the data collected during my research project, when comparing the prices of originator medicines between Jordan and UK, the statistical outcomes showed that the prices of originators in Jordan are 1.21 time higher when compared to that in the UK.

Examples:

- Gastro-Intestinal, H2 receptor :Ranitidine originator prices in UK 0.043 pound/ddd while in Jordan 0.308 pound/ddd
- Cardiovascular system, Angiotensin Converting Enzyme inhibitors lisinopril originator in UK 0.073pound/ddd while in Jordan 0.419 pound/ddd.
- Cardiovascular system, beta blocker Metoprolol originator price in UK 0.138 pound/ddd while in Jordan 0.412 pound/ddd
- Eye drops, Cartelol (betablocker) originator price in UK 4.6 pound while in Jordan 9.106 pound for the same drop size.
- Eye drops, travoprost (prostaglandin analogue) originator in UK 20.34 pound while in Jordan 27.125 pound
- Bimatopros originator eye drop price in UK 17.167 pound While in Jordan 22.548 pound
- Hormone antagonist Letrozole 2.375pound/ddd UK while in Jordan 5.045 pound/ddd

In your opinion, what might be the reasons behind this?

- According to the statistical analysis of some of the data collected during my research project, The prices of generic medicines prices in Jordan for all generics

drug sample which available in both countries are 2.17 times higher than in the UK. Taking into consideration that the yearly income per capita is 7 times lower in Jordan.

Examples:

- Central nervous system, control of epilepsy: Gabapentin generics average price per ddd in UK 0.331 while in Jordan 2.354 per ddd
- Central nervous system, Selective serotonin reuptake inhibitor citalopram generics: 0.047 pound / ddd UK in Jordan 0.466
- Cardiovascular system Calcium channel blocker amlodipine generics: 0.04 pound/ddd while in Jordan 0.318 Pound/ddd
- Cardiovascular system Alpha blocker doxazosin generics 0.058pound/ddd while in Jordan 0.401 pound/ddd
- Cardiovascular statin pravastatin generics average price per ddd in UK 0.196 while in Jordan 1.766 per ddd
- Cardiovascular statin simvastatin generics average price per ddd in UK 0.102 while in Jordan 0.711 per ddd
- Gastro-Intestinal, proton bump inhibitors lansoprazole generics price per ddd in UK 0.107 while in Jordan 0.759 per ddd
- Gastro-Intestinal, proton bump inhibitors omeprazole generics price per ddd in UK 0.063 while in Jordan 0.682 per ddd

In your opinion, what might be the reasons behind this?

- Is it reasonable to price generic medicines at 80% of the price of their originators?
- is the cost of locally produced generic medicines counted for 80 % of that of their originators?
- How does the export market affect the prices of locally produced medicines?
- What is your targeted market (local or export)?
- How does the pharmaceutical companies' bonus and incentive to pharmacists influence the prices of medicine?
- Does the fixed profit margin (regardless of the cost of medicines) encourage the dispensing of higher priced medicines?

Example:

- Originator imported drug Famotidine PEPCIDIN 20mg, 30 tablets back: pharmacy cost: 16.1 public selling price no vat 20.29 net profit: 4.19 Jordanian dinar
- Generic locally produced Famotidine: Amodine 20mg, 30 tablets back: pharmacy cost 3.37 public selling price no vat: 4.25 net profit: 0.88 Jordanian dinars

- How does the cost of promotional activities carried out by pharmaceutical companies would affect the requested proposed price?

- What do you think of introducing a generic substitution policy?

- How would the introducing of generic substitution policy affect the pricing of medicines?
- What do you think of introducing an INN automated prescribing system?

- How would the introducing of international non priority name INN automated prescribing system affect the pricing of medicines?

Closing:

I appreciate the time you took for this interview. Is there anything else you think would be helpful for me to know?

Thank you for your cooperation

Appendix 5

Interview Schedule for Pricing Authority

Opening:

- Introduce myself and give a brief about my PhD research

Body:

- Do the prices of medicines in Jordan reflect the effectiveness of the current pricing policy, and why?

- [prompts] In terms of availability and affordability of medicines?
- [prompts]In terms of availability of cheaper generic medicines?

- According to the statistical analysis of some of the data collected during my research project, when comparing the prices of originator medicines between Jordan and UK, the statistical outcomes showed that the prices of originators in Jordan are 1.21 time higher when compared to that in the UK.

Examples:

- Gastro-Intestinal system, H2 receptor :Ranitidine originator prices in UK 0.043 pound/ddd while in Jordan 0.308 pound/ddd.
- Cardiovascular system, Angitensin Converting Enzyme inhibitors lisinopril originator in UK 0.073pound/ddd while in Jordan 0.419 pound/ddd.
- Cardiovascular system, beta blocker Metoprolol originator price in UK 0.138 pound/ddd while in Jordan 0.412 pound/ddd
- Eye drops, Cartelol (betablocker) originator price in UK 4.6 pound while in Jordan 9.106 pound for the same drop size.
- Eye drops, travoprost (prostaglandin analogue) originator in UK 20.34 pound while in Jordan 27.125 pound
- Bimatopros originator eye drop price in UK 17.167 pound While in Jordan 22.548 pound
- Hormone antagonist Letrozole 2.375pound/ddd UK while in Jordan 5.045 pound/ddd

In your opinion, what might be the reasons behind this?

- According to the statistical analysis of some of the data collected during my research project, the prices of generic medicines prices in Jordan for all generics drug sample which available in both countries are 2.17 times higher than in the UK. Taking into consideration that the yearly income per capita is 7 times lower in Jordan.

Examples:

- Central nervous system, control of epilepsy: Gabapentin generics average price per ddd in UK 0.331 while in Jordan 2.354 per ddd
- Central nervous system, Selective serotonin reuptake inhibitor citalopram generics: 0.047 pound / ddd UK in Jordan 0.466
- Cardiovascular system Calcium channel blocker amlodipine generics: 0.04 pound/ddd while in Jordan 0.318 Pound/ddd
- Cardiovascular system Alpha blocker doxazosin generics 0.058pound/ddd while in Jordan 0.401 pound/ddd
- Cardiovascular statin pravastatin generics average price per ddd in UK 0.196 while in Jordan 1.766 per ddd
- Cardiovascular statin simvastatin generics average price per ddd in UK 0.102 while in Jordan 0.711 per ddd
- Gastro-Intestinal, proton bump inhibitors lansoprazole generics price per ddd in UK 0.107 while in Jordan 0.759 per ddd
- Gastro-Intestinal, proton bump inhibitors omeprazole generics price per ddd in UK 0.063 while in Jordan 0.682 per ddd

In your opinion, what might be the reasons behind this?

- Is the current ceiling price (80%) one of the reasons behind the high price of generic medicines which are mostly locally produced medicines?
    - Why 80 %?
- How does the export market affect the prices of locally produced medicine?
- Targeted market (local or export)?
- How does the pharmaceutical companies' bonus and incentive to pharmacists influence the prices of medicine? (Reminder for interviewer: Generic manufacturers over price their products so when they give bonuses and incentives they will still make profit)
- Does the fixed profit margin (regardless of the cost of medicines) encourage the dispensing of higher priced medicines?

Example:

- Originator Famotidine imported drug PEPCIDIN 20mg, 30 tablets back: pharmacy cost: 16.1 public selling price no vat 20.29 net profit: 4.19 Jordanian dinar
- Generic locally produced Famotidine: Amodine 20mg, 30 tablets back: pharmacy cost 3.37 public selling price no vat: 4.25 net profit: 0.88 Jordanian dinars

- How does the cost of promotional activities carried out by pharmaceutical companies affect the proposed price?

- What do you think of introducing a generic substitution policy?

- How would the introducing of generic substitution policy affect the pricing of medicines?

- What do you think of introducing an INN automated prescribing system?
- How would the introducing of international non priority name INN automated prescribing system affect the pricing of medicines?

Closing:

I appreciate the time you took for this interview. Is there anything else you think would be helpful for me to know?

Thank you for your cooperation

Appendix 6: Interviews Transcripts

R1:

- **How efficient is the new pricing policy? How far did it affect the pricing of medicine?**

-For the reference states that have been added, we had 7 reference states in the older rules but now we have 16. We take Media as having been of no use. Even some prices soared adding more burdens on us and making procedures more complicated without reducing the prices. Some added states have low prices but the problem was in using the Median. The preliminary suggestion was to adopt the average of prices of the lowest 4 states out of the total 16. However, this suggestion has not been approved of yet by the Higher Commission so we had to take the Median for the 16 countries, which had large effects on the pricing.

- **You mean if we take the average, things would differ?**

-I do not believe so. The preliminary suggestion was to recommend the use of the average of the lowest four states. However, pressures were exerted on the pricing committee by the originator and generic companies, the latter of which define their prices based on the originator's.

- **Should the pricing policy's effect be different than that?**

Yes. Honestly, it added to our work load. Some medicines' prices were reduced including contractual medicine produced abroad for the interest of a local Jordanian manufacturer. The result is that we take 70% of the originator's price, which reflected on lowered prices. This means that upon the request of the company or the respective price in Saudi Arabia or in the reference states (the median states), the originator's price is now lower based on the country of origin, the median or the Saudi price. In the past, the practice was that if a medicine is imported we would not reduce the price of the generic medicine. With the application of the new rules, when price is lowered even if it is not imported, we lower it. This affected the lowering of price of the generic medicine.

We have also pricing based on concentrations. I have a concentration table that defines prices, which lowered, though to a little extent, the prices.

- **Also, the issue of medicines composed of more than one active ingredient?**

-Exactly. Here 10% is deduced from the respective prices of the active ingredients in case each medicine is purchased alone. This helped in reducing the prices. However, medicines that are already registered cannot be subject to the concentration table, which only governs those medicines registered after the introduction of the rules.

- **What about prices and the Median states' issue? When will they be considered?**

-When we register a new medicine in accordance with the 16 states.

-When a new originator is registered for the first time, this rule (Saudi Arabia plus the 16 states) will apply.

- **What about older medicines?**

-After two years of their registrations. But after the lapse of five years of their registrations (when renewal is due) I apply the rule. The originators, when registered for the first time, will be subject to the rule. After two years of their registrations, I review them in light of the same rules then after five years of registration (i.e. when renewing them) I review their prices.

The medicine is now traded in the market. Then, I follow up with its pricing every five years unless the respective price is decreased in the country of origin or in Saudi Arabia, in which case I need to be informed of that. If such a period elapsed without my revision of the prices and that the prices of the medicine in the country of origin has decreased, he must inform me of that to reduce his price accordingly. Failure to comply will impose on him fines.

- **How can you figure out that the price has deceased? How do you tell whether or not he has informed you?**

- At the beginning of every year, a circular is sent to stores asking them to inform me of the prices of the country of origin and the prices in Saudi Arabia if such prices have decreased. Then the stores should communicate with their respective companies and receive answers. Now, the answer is supposed to tell whether or not the prices have decreased. The company knows now very well that if it fails to notify me of that decrease within four months of the date of decrease in Saudi Arabia or the country of origin, it will be subject to a fine. So, they are now informing us of such decreases of their own motion.

- **Is there any cooperation between you and the Saudis in respect of pricing in Saudi Arabia?**

-Yes. At the beginning of every year, we receive lists of prices, which we review.

- **If you review the prices you find a difference, will the fine apply?**

-If there is a difference that I was not notified of by him within four months, he will be fined. If the four-month grace period has not elapsed yet, I do not impose a fine on him.

- **Does the same apply on generic Jordanian drugs?**

Just the imported generic. This does not apply to the Jordanian product because it is governed by the older rules, which did not provide for an obligation to inform me of the Saudi price. The new rules have included such a provision but the Jordanian Union of Medicine Manufacturers requested us to revoke this provision because they were not provided for in the older rules.

- **This means that the price of a medicine in Jordan is defined in relation to the genereic's price in the country of origin for which reason it becomes high for exportation purposes since every importing countries considers the price in the country of origin.**

This is the policy in all countries in the world. Reference is made always to the country of origin. For example, Jordan makes a condition for every medicine that its price in the country of origin is higher than that here. The Jordanian medicine follows the same rule.

- **This means that we, as Jordanian consumers, are not benefiting of the Jordanian medicine manufacturing because their prices should be less but their price is high for exportation purposes.**

-They do not raise the price deliberately. We give them a ceiling that is 80% of the originator's price. Also, when the originator's price decreases, the Jordanian product decreases too as is the case with other generic products.

- **But when considering the current pricing rules in Saudi Arabia, they provide for 70% for the first time then it gradually decreases. Is it difficult for us to do the same thing?**

-We would not do that for otherwise the Jordanian manufacturers will rise and say "Support me and support my industry and I will in turn export products."

- **To support the Jordanian medicine products, we do not you resort to two pricing lists for example?**

-I cannot issue a certificate for him.

- **Why not allowing him to have two trade names?**

-I cannot provide any false information. The information I give out must be true because we are the Ministry of Health and must be a source of credibility.

- **What is the solution? Is it to make the generic medicine of lower prices?**

-We tried that. I told you as for the Jordanian medicines, some products have been lowered in price because the contractual medicines are for those Jordanian medicine manufactured abroad.

- **This applies to the locally manufactured products as is the case with Al-Hikma's medicines?**

-No. This is not what I meant. Now, we are working with the new rules of JBM medicine. Al-Hikma is manufacturing through factories abroad but the holder of the marketing right in Jordan makes the secondary packaging locally. For example, A JBM has several products manufactured abroad. It registers them in India then makes secondary packaging for them in Jordan in a JBM factory. Now, according to the new rules, we given them 70% rather than 80% of the originator's price. This means we have slightly lowered the price of the Jordanian medicine.

Now, according to the older rules, when I review the price in the country of origin like Amaryl, which is made in Italy and whose secondary packaging is handled in Jordan, a provision stated that I do not review its price in Italy. But, now we have new rules that require me to review the price in Italy, which eventually helps in lowering the price of the medicine.

Let us assume that I have a GSK originator from Britain. I will not review its prices in Britain. The agent may give me prices in 16 states that do not include Britain, the country of origin.

He must give it give me that piece of information. If he does not comply, I will get into the electronic website and get it. I will not solely rely on him to give me the information I need. Even if he brings me the information, I verify and the officers here verify it through the electronic websites.

As for the Jordanian, no. In light of the new rules, he must inform me of the Saudi price but at the moment, local factories represented by the Jordanian Union of Pharmaceutical Manufacturers have requested that we do not apply such a provision. I asked the Minister to amend the provision. Though we do not necessarily have to comply with their requests, we have not so far enforced that provision (I mean to review the price of the product in Saudi Arabia and apply it to the Jordanian product).

- **But if you do that, the prices will sharply drop because the Jordanian medicine for such a company as Al-Hikma has been exported to Saudi Arabia and will take 70% of the originator's price, which eventually leads to that price drop.**

-Exactly.

- **When I embarked on my study on all medicines that treat chronic diseases I came up with over 320 medicines. I noticed that prices for the originators are overall much higher than in Jordan. A statistical analysis showed that Jordanian medicines are 21% higher than in Britain.**

  For example, Zantac in Britain costs 0.043DDD while it is 0.308 in Jordan, meaning an 8-fold the price in Jordan despite the fact that Jordan's per capita income is less than that in Britain.

-Supposedly, the price in Jordan is less because the country of origin is Britain. We calculate according to the court of origin

- **Perhaps the price dropped in Britain after its registration in Jordan but has not been reviewed since then.**

-But there is a consideration of the value added tax (VAT), which accounts for a difference between the two countries. It is a difference of 16%

- **Vat in Jordan is 4% but it is 20% in Britain but I compared the public prices with no vat**

-The comparison is not fair because the profit rates here are different from those there.

- **I am drawing a comparison from the consumer's perspective. Our income levels are much lower and medicine is higher in price. For example, Dezinopril price is 0.037 in Britain but it is 0.419 in Jordan. This means that if we have 30 pills, then their price is around JD12 while it is there 2.1 (same unit at DDD**

currency) which means that the medicine is 6 times higher. This concludes that there are overall lots of medicines, not to mention eye drips, are much more expensive.

-This calls upon us to review the rules. They are flawed.

- **Exactly. You may even consider changing the rules by envisaging external powers that interfere in the matter.**

-Of course. When we laid down the rules of pricing, we had two representatives from abroad. Therefore, when I adopted the Median principle, I would take into consideration the lowest 4 countries that are fighting with us and had consequently to submit to them.

- **How do you explain that originators' prices are much higher than in Britain?**

-As I told you it is the rules. However, we look at the prices of the originators in the UK and we do not find a significant difference. But it turns out that we are taking prices as if we were in Europe. My reference is Saudi Arabia and Europe. We are talking here about high-income countries while Jordan is a low-income country. Our problem will not be solved because the solutions that we have in hand are only partial unless a comprehensive medical insurance is provided at a cheap price. For example, the state will take Zantac for all the people then enter into a tender at very cheap prices. I mean that the price given in a tender is very low but when the medicine is sold in the market, it is expensive. This is their argument.

- **Even the price given in a tender is meant to market the spread out the product.**

-Afterwards, the price soars or the insured patient has to purchase the medicine from the private sector at own expense. This is one way of marketing and penetration strategy.

- **Also, when I made the statistical analysis, the generic medicines were overall higher 2.17 folds of the price in the UK. This is as far as a group of drugs are concerned. However, some medicines are 15 fold higher in price than in the UK including for example the Jordanian generic escitialopram, which is 15 fold higher in price than in Britain although the per capita income of Jordan is significantly lower.**

-Please send me this study so that I use it and discuss the rules with them.

- **Originators in general in Jordan are as a whole 22% higher though some medicines are higher than this rate. The generics on the other hand are two or more folds that is about 22%. Some medicines are even 8 or 15 folds. Why?**

- The rules give a high price for the originators and therefore I am surprised that the generic is in such a situation its price being derived in the first place from the selling price in Jordan. Here in Jordan there is no competition. Everyone is happy with the high price and are reluctant to reduce it. So it becomes like an implicit agreement as if they were saying to each other: this is my 80% so please do not reduce our price to less than this one. This means there is no competition.

- **Are there any medicines that were requested to be registered at less than 80%?**

-It is only when he requests so. There are medicines less than 80% because I look at 80% of the originator's current price in the renewal of registration. This gives less than 80% of the current originator's price because it is registered and priced according to the older originator's price. It is however very rare that the price is less. Very few people requested that. There must be a competition in prices between local companies.

- **Why 80% and not 70% as in Saudi Arabia?**

-It was 70% in the proposed rules but was changed into 80% under the pressures of factories and the Jordanian Union of Pharmaceuticals Producers so the rate returned to 80%.

- **Even 70% and 80% are high. The originators' companies conduct lots of research and spend a lot on the. Some of their medicines succeed; others fail.**

-But, the originator that is imported from abroad is less than 80% because in the country of origin, control departments control prices but in Jordan almost all generics' factories price at an 80% basis.

- **But Jordanian factories are not burdened with expenses on research and development, which raises questions on the pricing of generics in Jordan targeted markets and exportation markets?**

-Exactly. They do not care about the Jordanian market.

- **On the bonus issue, when a company grants a 100% bonus it means that when for example the medicine is priced at JD5 it has sold it to you at JD2.5 and still made a profit. This means that the prices are not real but higher than the natural price.**

-This means that they are using the bonus rather than the price itself for competition.

- **Exactly. It is bypassing! What will happen if the bonus is abandoned as in the case of the United Arab emirates?**

-In Saudi Arabia, it was abandoned. We did the same for some period of time but will consider it. It needs to be controlled.

- **I think you will not be able to abandon the bonus because of the 70%/80% and 4-months consideration that did not work and because of the external pressures. Why are those pressures exerted on you?**

-Pressure is exerted on us by local producers. Even on the originators there is a pressure. When we changed the Median to take 16 instead of 7, they put on lots of pressures until I had to take the median on no less than 4 states. It is because they are the ones to benefit.

- **What about the fixed profit (26%) of the pharmacy? For example, the originator Famoditine (20 mg, 30 pills) costs 16.1 for the pharmacy. The selling price (without the 4% vat) is 20.29. This makes the net profit for the pharmacy 4.19. As for the generic counterpart with the same specifications it costs for the pharmacy 3.37. it is sold at 4.25 making the profit as little as 0.88. If I were a pharmacist, I would think of selling the originator to gain more profit. Have not you though of setting a margin for profit based on the price of the medicine?**

-We did. We are now considering the fact that profit rates change and become in categories. Expensive drugs have lower profits and those with little profit will have higher profit margins. No development has been made on this issue yet because we are already busy and we have been affected by the change of directors. Every director comes with different thoughts and trends. Our current director is new to the department. Within 8 years, we have had 4 directors. Even the director of a department in JFDA was in the ministry and they appointed her here.

- **It is noticed that pharmaceutical companies (originators and generic) do lots of promotion with pharmacists and doctors. Does this promotion affect the price of a medicine?**

-Sure. People at the end of the day pay for that.

- **Cannot you restrict such promotions?**

-As for the specimen, there is a code of ethics followed by the companies. We need to work on the bonus.

- **What about the substitution of medicine by pharmacists (from originator to generic)?**

-It was proposed but I am not sure if they introduced it to the law.

- **If it has to do with the Jordanian law, pharmacists cannot do that except after consultation with the doctor. By the way, in western countries, a doctor is not consulted for such a matter except in specific drugs like the Digoxin. If we introduced this policy, this would reflect on the prices and people so that they can choose the cheaper medicine?**

-We here come back to the bonus issue. The one who gives you more is the one whose products you sell more. It will not make a difference in price for people. People will not benefit at all. What we need is a pricing policy that sets low prices or alternatively as you suggested a comprehensive medical insurance plan should be put in place so that all pharmacies are contracted with and companies will compete in the same manner as in the western countries.

- **What do you think if the prescription is given by writing the scientific name and the cheaper substitute drug to be given?**

-This unfortunately needs awareness raising campaigns and out people to be well informed.

- **In the UK, I go to the doctor's. When the doctor wants to prescribe a medicine he uses the computer and through a specific system he can choose the cheapest medicine that has the same scientific name. Is that all impossible in Jordan?**

-We hope so

- **Would it be better to be fully connected to Saudi Arabia?**

-No. It does not serve my interests. Lots of medicines are registered in Saudi Arabia at cheaper prices and once the companies made a suggestion that they accept the prices of Saudi Arabia. But the older medicines are much cheaper than in Saudi Arabia and it is we that started before Saudi Arabia. Saudi Arabia later adopted a very good plan in respect of the generics, i.e 70% then lower and lower.

- **The same is here, right? I mean we do not change the prices of the older medicines?**

No. We change the older medicines after give years of registration. But take into consideration that while Saudi FDA has 45 employees working in the pricing department alone, we have only five employees here working on the reduction of prices not to mention the huge load of work that we have and the inappropriate place and administration in addition to poor salaries.

- **In your capacity as a secretary general, are the pricing rules satisfactory for pharmaceutical companies?**

-Yes. They are good and balanced despite some flaws. Early rules emerged in 2004. Then, they were amended in 2005 and 2012.

- **What do you think of the current rules?**

-We have some remarks but generally they are clear, which is very important. Sometime clarity is reduced but in every state of the exportation market we followed the state that can make expectation. Clear rules are essential to inform your decision on what to manufacture and what to not manufacture. They also tell you how much sales you expect. This will make companies have clearer strategic planning for defining prices in Jordan in comparison with other markets. Jordan is the country of origin, which will be the starting point for me to enter all markets. When deciding the price of a given medicines, some items and operation rules will help me understand what to do and when to change the price in a shorter period of time to recover costs incurred in the investment in the medicine.

- **In principle, the aim of the pricing policies in Jordan and worldwide is to achieve medicine security. Do you think such rules have indeed achieved medicine security?**

-Medicine security is the responsibility of the state rather than the private sector companies. Second, medicine security is achieved when a comprehensive medical insurance scheme is put in place. You cannot therefore take a particular issue of the medicine price in the private sector to judge whether there is or not such medicine security. This does not apply to states that are implementing a coverage scheme to ensure the health welfare of citizens. Comprehensive health systems must be introduced to achieve the aspired security.

- **Not only citizens but also residents on their lands as in the UK are covered. I myself am covered by health insurance. In contract, lots of people in Jordan are not insured but still there are government treatment exemptions.**

-According to Ministry of Health's statistics, 75% of the Jordanians are insured. This I believe is a good rate. The non-insured are mostly insured by the private sector or a royal initiative. So you are talking about an industry that starts in Jordan. The nature of pricing in the Arab world is to consider that the price of the public of the country of origin is the selling price for other markets. Furthermore, you have to look at the issue from a wider perspective. I mean what interests you should be the country being of economic strength. You will not look for a country that suffers from high rates of employment while medicine is cheap. What you need is a country that has strong economy where people can work and buy the medicine at moderate prices. We cannot therefore stick to the issue of pricing alone. We should study it from all angles. With this issue, figures alone do not work and it is not correct to simply say "This medicine is expensive so let us reduce its price" and make it like in Britain. Is lowering the price in the interest of Jordan? At the end of the day,

we care all Jordanians and care about our country's welfare. How come that Jordan becomes strong without a strong economy? We also have to remember that pharmaceutical companies in Jordan are private and not public companies as in the case of Egypt and Syria. Our companies are profit-seeking companies. Who will pay for the price? It is the citizen and the government. It is an interlaced cycle that has to be studies when considering the prices of medicine in Jordan. We should look at the matter from a holistic point of view and avoid using one perspective (uninsured patients do not account for more than 14%) in prejudice of other ones.

- **What about the latest pricing policy? And using Saudi Arabia as a reference country for some medicines**

-First of all this is not new. In 2004, there emerged the first principles with a Saudi item. The next amendment in March added that the Saudi prices are the term of reference for pricing medicine in Jordan (Jordanian and non-Jordanian medicine). This did not apply. I mean the imported medicine was exported to 20 states. If Saudi Arabia is one of those countries they consider the price in Saudi Arabia when registering the Jordanian medicine. Afterwards, the medicine is registered in Saudi Arabia but now there is no sate in the world that takes the prices of its local medicine in exportation markets as a term of reference. A simple amendment was made in Jordan:

- **All Jordanian medicines are prices at the basis of 80% of the price of the originator? Why not less than this ceiling?**

-I can cite some examples about companies that required less than 80% of the originator's price. The issue has to do with the company's strategy. If it is based on the price in the Jordanian market it takes less than 80% but for exportation it takes 80% because all states require the price of the country of origin first then it is negotiated.

Example: an Originator is priced at JD10 in Jordan. If priced at the basis of 50%, it will become JD5 in Jordan but when exporting the medicine, there will be negotiations to reduce the price less and less. This is why all are requiring the ceiling to be 80%.

- **This means you can achieve your profit in both cases: 80% and 50%?**

-80% of the originator's price in a small market like Jordan achieves for me less profits that those achieved by the 50% rate in a gigantic supply-demand market like Saudi Arabia.

- **Is the external market the one that is targeted by the Jordanian industries?**

-The Jordanian market is very small. I have to care for exportation markets. If the pricing of Jordan is linked to exportation to Saudi Arabia automatically, the price will be reduced in Jordan accordingly. This is because the price in Saudi Arabia for the generic is priced in a decreasing manner: from 80% to 60% then 50% of the originator's price. Then it is fixed. For example, when a Jordanian medicine is registered for the first time in Saudi Arabia, it will take the price of JD5 so it has to be decreased in Jordan to JD5. Then if I want to re-export it to Saudi Arabia or any other Arab country, I need to decrease the price. In

addition, we sell in tenders at much lower prices compared to prices sold in the private sector.

The Jordanian industry will sustain losses accordingly and the capitals and factories will move from Jordan because the price in the country of origin like Saudi Arabia will reduce our prices in all exportation countries. With every freight of medicine, they ask us to provide them with the price in the country of origin. In contrast, the generic Saudi or imported medicine will take 80% of the price of the originator. This means that it will make more profit without employing nationals. The result is that investment is not made in Jordan. Why?

- **How can you afford it? You sell some medicines in tenders at as low as JD1 while they are sold at JD8 in the private sector.**

- By selling medicine through tenders I achieve lots of benefits. I make my product known to people even if I do not make lots of profit. A tender means that I give supply bulk quantities solely to one procurer, that is governmental warehouses. This spares me transportation expenses that would otherwise be spent on transportation to the various parts of the country. It spares me marketing and medical care costs. In addition, manufacturing costs for me in tenders are lower than usual. The same applies to labeling. In contrast, if I have to export to other Arab countries, I have to meet some requirements including for instance printing the pamphlet in English, Arabic and French as in the case of Algeria. In tenders, I supply 100 pills in one pack rather than 30 pills as required for exportation.

Cleaning the machines also cost less with tendered medicine. If the tender requires four million pills, it will not be necessary clean the lines on a daily basis. In contrast, we need to clean the machines every day for different manufactured medicines, which incurs a high cost.

- **What do you think of Saudi Arabia as being a term of reference for Jordan?**

-It is an indicator that benefits Jordan in some cases. However, you cannot compare their prices with ours. The pricing methodology is different here.

- **Do you look at the foreign market when defining the price of a product?**

-Sure. I need to see the target market and the markets available to me and now much it is priced here and there in addition to expectations on sale volume.

- **Is it really just 20% of the value of the medicine that accounts for research and development? Everybody is pricing at an 80% basis?**

-In Jordan, there is no research and development. There is development. Even when you manufacture the generic medicine, you need to know the right composition and concentrations until you arrive at an equivalent formulation.

- This is made only on 300 millions in Europe and the same amount in USA. There are some multinational companies that sell in the Arab world alone not to mention the Jordanian market.

I agree with you that the costs of the research and development are very high and that the originator's costs take into consideration the prices of the failed experiments. That is you put 100 products to get one so it means that you add the cost of 200 to the next product. But he can recover the costs because he will buy the product alone in the market for a considerable long period of time.

When we take the up-to-80% rule, most ask for 80% but still some ask for less. For example, ciprofloxacin is registered and started in Jordan with a cost of JD10 or JD8 and ended up with JD5.

- **I suggested to JFDA that if they sort out the problem and support local industry while at the same time we subsidise products for uninsured people. I suggested for example to allow them to register two trade names for the same product, one for Jordan called revanin for example and another called revalieov for exportation?**

-I cannot see anything wrong in that. Each product will have its own invoice and price.

- **In this way, we can increase the price to higher than 80% and support the factory?**

-I am not sure of the companies or exportation markets will accept such a practice. The world is small and people will know about it. I do not know if anywhere else in the world such a practice is followed.

All Arab governments support their own companies. In Algeria, it is forbidden to import generics in case there are two Algerian producers. The same applies to Egypt. The Jordanian industry has benefited a lot from the deteriorating circumstance in the country and managed to prove themselves despite all difficulties.

To enter the Algerian market, Jordanian factories had to open up factories in Algeria. Currently, there are four Jordanian pharmaceutical factories in Algeria. This is because of the laws protecting factories there.

Egypt allows for the originator and the generic but with a ration of 1 (imported) to 10 (Egyptian generics) unlike the practice in Jordan. Some medicines have more than 25 generics locally made and imported.

- **I found out that the originators are expensive but not as expensive as the Generics?**

-When you say that 30% or above depending on the specimen that you have (out of 320 medicines), I once again say that you are comparing this with Britain. Britain does not have tenders or private sector. The market factors are totally different and the market there is open. You cannot compare prices without referring back to the other factors if you want to make a balanced comparison.

- **Britain is a developed country. We need to benefit from its experience. It is also a rich country and its per-capita income is around 7 fold higher than that in Jordan. Still the price there is less than is here?**

-The per capita income will be better and so will be the Dinar's value if we have a strong industry and economy in the country and if we have more exports. The pharmaceutical industry in Jordan is one of the most important industries. It serves Jordanians in terms of numbers of employees there and the benefiting families. We need to consider also the high power supply costs in Jordan compared with those in the region. Pharmaceutical factories also serve the local community.

JFDA's rules are very strict. They follow the international standards and adopt some laws of the United States and the EU. This is why registration in Jordan is very difficult. A Jordanian medicine for example was registered in France but could not be registered in Jordan. The rules in general must be revised to meet the needs.

- **What do you think about the Bonus?**

-100% marketing tool.

- **But it does not have any bearings on customers?**

-What are the marketing tools used by Jordanian pharmaceutical companies in Jordan and abroad? When a doctor and his family and children travel abroad, will this reflect positively on the consumers! In fact, the doctor will come back home and prescribe for patients the expensive medicines. Sometimes also bonuses are exaggerated if the bonus giver is making lots of profit. The matter is in the hand of the pharmacist.

- **Legally speaking, the pharmacist has no say in it.**

-I am not talking about the law. I am talking about daily practices. Practices reflect the current authority. The generic entitles him to a bonus and the originator entitles him to privileges and travels.

- **So, the Jordanian factor that gives a 100% bonus for a JD8 medicine means that the price is wrong and that it should originally be JD4?**

-Instead of giving a trip to the doctor and his families like the foreign companies do, I give a bonus to pharmacists.

- **What do you think about the profit margin made by pharmacists? It is fixed. How about famoditine as an example?**

-I agree with you. It should not be the case that for a JD100 medicine the pharmacist gets JD26. It is a high rate. There must be segments of profits depending on the price of medicine that must be decreasing when the price gets higher.

- **How about advertising and promotion?**

-Surely all of them add to the costs. They are not related to the price of the medicine but to the profit making. The price of the medicine cannot be higher than the 80% rate.

- **What about introducing a generic substitution of medicines (originators by generics)?**

-This is a mistake because it will add to the power and control of the pharmacist. It will only benefit the pharmacist.

- **How about writing the prescription using the active ingredient's name?**

-This will be fatal for the Jordanian industry. The main feature of this industry in Jordan and in the Arab world is that they are branded generic.

For example the trade name of Coca Cola is Assets. If a prescription is given in the scientific name, it will kill the local industries. The future of global industries will be towards the branded generics. Prescriptions made by using the scientific names of the medicine will give much more power to pharmacists added to the bonus pressure. The patient will benefit nothing.

Jordanian pharmaceutical companies are the future of our country and we must care for them.

- **What do you think of current pricing?**

-As Jordanian pharmaceutical company, these prices are up to our aspirations. This is because we adopted the price of the originator medicine, which amounts to 80% of the originator's price. This is an excellent price for us because the originator is usually very expensive.

- **All factories consider 80% as the highest rate possible. A factory rarely asks for a price less than 80%. Why?**

-To get the highest price so long as this is legal while keeping at the same time for myself a margin of-20% to compete with the originator.

- **Competition in your case is with the originators rather than the similar generic medicines. Right?**

-There is competition but in quality. Most prices of the generic medicines are almost the same (with a slight difference margin of 3-5%). The price is an important factor in competing with the generic medicine but its role will be clearer when competing with the originators.

- **What do you think of Saudi Arabia as a frame of reference for pricing in a country like Jordan?**

-Honestly, comparing Jordan to Saudi Arabia with regards to linkages between medicine and pricing can be fair. The Saudi society is very large and has a per capita income close to that of Jordan. Yes, there are extremely rich Saudis, but the majority's per capita income is similar to that of Jordanians if not less in some cases.

Incomes are similar and so are the prices. I noticed that in the IMS on prices. This is unlike other markets that show high prices of medicine.

Somehow, reliance on the Saudi market is far but I am waiting. In light of my knowledge of both Saudi and Jordanian markets, prices in Saudi Arabia can be higher than in Jordan and vice versa. Pricing medicine in Saudi Arabia depends also on the originator's price as is the case in Jordan.

- **Their pricing standard is 70% for the originator. Subsequent registrations of medicines take fewer rates up to 50%. Jordanian medicine will not be the first to be registered there. Hence, your price will be 70% less than the price of the originator as you know the Saudi market's size is very large compared to that of Jordan, particularly if we take into consideration the pilgrimage and Umra seasons. This means that the price of the originator will be less than the price of the originator in Jordan. Therefore, inevitably, your medicine in Saudi Arabia will be less?**

-This is a principle in Saudi Arabia and Saudi laws. The other factors, however, is related to your price in Jordan (price given by the country of origin plus the freight fares) then follow the negotiations.

- **On what basis do you price the medicine for the Jordanian market (factors)?**

-Price for me is fixed and is defined through the 80% difference with the originator's price. Before manufacturing any medicine and sending it to the market, we rely on the 80% price of the originator's. The price is fixed. Then I look at the costs and expenses incurred by manufacturing, promotion and marketing. The net profit is usually very high.

- **Prices of originators compared with those in Britain taking into consideration the fact that Jordanian incomes are much lower than those in Britain. For example: (as in the interview schedule).....**

-In my opinion, the price of the originator is usually high. This is because of manufacturing reasons. For example Zantac which exists in Jordan.

-The same British line of production. There are no international originators' factories in Jordan, which directly imports such medicine from Britain. This increases the cost of its manufacturing and adds other expenses including staff salaries equipment, power supply, transportation and marketing among other things. These costs are the same that are added to the price of the originator in the UK in addition to the agent's profit. This is why the originator is naturally expensive.

The Jordanian market is not a significant one neither is it targeted by originators' companies or the Jordanian generic companies.

The Jordanian market is very small compared with international markets. This is why the price here is much higher.

- **How do you compare Prices of the generic medicine in Britain and Jordan?**

-Jordanian companies are benefiting from the price of the originators and the principle of pricing that bound us to charge up to 80% of the originator's price.

Differences in pricing between Jordan and Britain are the biggest and main factor for that.

- **The pricing principles defined 80% as the ceiling of the price so why do not Jordanian companies price at a 40% or 50% for example?**

-But why should I not get the highest profit possible in respect of the Jordanian market? I also depend largely on exportation to other countries. Besides, importing countries require to know the price of the country of origin. The targeted market is the foreign market.

- **Do originators deserve a cost that is more than 80%?**

-No. The profit made by local companies is very high compared to the very low costs. The 80% rate serves Jordanian factories a lot because the productive cost is very low. I largely depend on the foreign market for exportation especially the Arab market, which requires to

know about the price in the country of origin. Jordanian laws are serving me, so why should I not benefit from them?

- **What about the Bonus?**

-Bonus is a marketing tool. Some generic companies may give a bonus of 300% and he still can make a good profit because of the little production costs of the generic.

One pack costs One Jordanian Dinar and is sold in pharmacies at JD24. In tenders, it is sold at 2.5 and still the company is making profit. The cost of the medicine depends on the cost of raw material in China or India. Basically, the production cost is very low and other costs relate to marketing. However, we can give a bonus to pharmacists or gifts to doctors. We can even afford doctors expenses for scientific journeys and conferences without compromising the ethics of the profession.

- **The profit rate of pharmacists is fixed in Jordan regardless of the price of medicine like Famoditine?**

-The fixed rate serves pharmacists a lot. This makes them eager more to sell expensive medicine, but this does not serve the people. This is the opposite to what happens in other countries like Saudi Arabia, which provides for categories of profits made by selling medicine. 50 up to 100 Rials has a high rate while 100 to 200 has a lower rate. This serves the patient. However, in the fixed profit rate system on Jordan, a patient feels a great discrepancy in prices. A pharmacist can also through the selling of the generic medicine make lots of profit particularly with the high bonus, so he can sell a medicine and have its total price as a profit if he obtained that medicine through the bonus system.

- **What do you think of generic substitutes?**

-I do not agree with generic substitutes except after consultation with the doctor or after taking the permission of the patient. This is particularly true if the patient is suffering from a chronic disease like cardiac diseases. The pharmacist is not entitled to such substitutions except with the approval of the doctor. As for OTC (over the counter) medicines like paracetamol, I think there is no problem in substitution without referring back to the doctor but the pharmacist at least should seek the permission of the patient.

Otherwise, if a pharmacist is given the full authority to substitute the prescribed medicine without referring back to the doctor, the substitution will likely be made in accordance with the interest and profit of the pharmacist rather than the interest of the patient. Unfortunately, not all generic medicines are of good quality in Jordan, which means the only driver for a pharmacist's substitution of a medicine is profit.

- **What do you think about advertising and promotion campaigns in Jordan?**

-I support such campaigns. This is competition. But promotion here in Jordan has infringed upon the ethical principles, which is a long-dated issue. I do not advocate non-ethical

promotion that has to do with the purchase of personal belongings or offering tourist (rather than scientific) travels. This has been severely destructive in our profession.

I am not with exaggerated marketing especially because it incurs additional costs on the companies, which consider them when calculating profit before offering the medicine. This cost is by the way not added to the price because as I know the ceiling is 80%. Some products are monopolized by some companies not because of high costs of production or difficulties but because some companies have better competitive edge and afford gifts to be given to pharmacists and doctors.

- **How about writing the active ingredient in medical prescriptions?**

I do not think it works. At least this has never been tried out in Jordan. If you do that, you are giving full authority to the pharmacist but as I said earlier, some generic companies are of low quality, which is not in the interest of the patient. Perhaps it works in other countries but definitely not in Jordan.

- **Are the current rules up to the ambitions of you as an owner of a pharmaceutical store?**

-They are good but the problem is in application, the rules care for the respective interests of originators and generics made locally. However, they fail to consider imported generics as those coming from Korea and India.

Local industry takes 80% of the originator's price but we ask that care is given more to the respective interests of medicine security, patients, the country and anti-monopoly practices. We need also to promote competition by removing the clause on dependence on the price of the manufacturer for the imported generic. For example, if they give us 40-50% of the price of the generic it is good. Alternatively, 60-70% of the local generic's price is good because it saves a lot for the patient. Rules are good but there is a problem in application. The rules preferred to serve foreign manufacturers of the originator (multinational companies) and Jordanian local generic industry companies.

- **What factors are observed in defining the price of medicine by pharmaceutical companies?**

-Generally, originators' companies provide for a base value. They put the price they want and Jordanian companies take 80% of the price. For the imported generics, we need to prepare the prices on an ex-factory basis, the public price and the price for exportation to Europe or Saudi Arabia. Most companies do not export to Saudi Arabia or Europe. This makes them depend on the ex-factory price. This makes the price considerably low. Some companies refuse such a price and deprive the Jordanian people from such medicines. Those medicines are turned out to be monopolized by virtue of the originator or the generic like Warfarin. If you import it from India, its price will be JD1.5. the originator's price in Jordan is JD4.80. Since Jordanian companies cannot make that medicine, the originator remains monopolized in the market.

- **What do you think of using Saudi Arabia as a reference company?**

Saudi Arabia is one of those countries adopted as a standard of pricing in Jordan the reason being that Saudi Arabia uses more than 33 countries in pricing while Jordan relies 16 only. I wish that the same pricing rules are used in Jordan. We note that prices in Saudi Arabia are 20% lower than in Jordan. If same rules are applied in Jordan, prices are to be less by 25% in Jordan. Lots of Jordanian companies refuse to register there.

- **The data pertaining to originators' prices show that they are less in Britain than in Jordan with an increase rate over 30%. (Examples as per interview guide))How do you account for that?**

-All international companies claim that Jordan's market is very small. This is untrue but it suffers from problems in applying the rules. The prices of such originators are decreasing worldwide but this decrease is not reflecting on a decrease in Jordan. The problem is in application.

- **The data of generic prices show that the prices are in Jordan 220% higher, though Jordan's income per capita is 8 fold less than that in Britain? (Examples as per interview guide)**

-Most generics in Jordan are locally made. The pricing rules state that the local industry takes 80% of the originator's price. The price of the originator must be controlled from the very beginner. The question is why does the Jordanian industry takes 80% . Egypt takes 60-65%, Turkey takes 50-60% and in Saudi Arabia, the price is gradually decreasing from 70% for the first time until 50%.

There is a mistake in the pricing rules, which provide for 80% of the originator's price. This is a high rate and is illogical. We agree that local industry should be supported but lots of medicines are not available because the local industry cannot produce them. What is the added value of the local industry? A drug like Ranitiadine has more than twenty generics but the local industry has no anesthetic medicine. You cannot find life saving drugs such as anti-cancer drugs because our local industry looks for the easiest produced ones and the most profitable.

- **Do you oppose the pricing of local generic medicines by taking 80% of the originator's price?**

-Yes. It does not deserve to be more than 50%. Also there is contractual importation where medicines are imported from abroad at very low prices then are packed in Jordan and their pamphlets are printed locally. They take 80% of the price of the originator.

I can procure the same medicine from China or India and wish to get 50% only. The clause on dependence on the ex-factory price should be abandoned. This is local industry and I am a Jordanian company. All staff in my company are Jordanians. He is a Jordanian investor and so am I. The problem in Jordan is that both the industry and the government are against the interest of the people.

- **What are the reasons for increasing prices by local industry? Is it because they are relying on foreign exports?**

-Jordanian industry is too much spoiled. That is the reason

.

- **What do you think about the bonus. Some companies give as high as 200% as a free-of-charge bonus.**

-This is a mistake. There are more than 21 local producers who make the same product. They are in competition. If I had the authority to define the manufactured products, I would have eliminated the bonus. This also means that the 80% is too much exaggerated. To give you a quick taste, compare the prices with those given in tenders. Sometimes, such prices in tenders are even as low as 50% of the price sold to people.

- **Pharmacies make fixed price margins as in the case of Famoditine (Example as per interview guide) In some countries, the higher are the prices the lower is the profit margin.**

To sort out this problem, here is a need to impose technical fees on the disbursement of a medicine as in the case of a doctor who charges for diagnosis at fixed prices. In relation to the above example, the profit gained through the bonus can be compensated for by the technical fees of the pharmacist for each prescription.

- **What do you think of promotion and marketing campaigns in Jordan? Do they affect prices?**

In all countries, companies use all means possible (clean or dirty) to get profit. There is a code of ethics in Jordan but is not observed. This also relies on the type of doctors. This is not controlled. There are lots of registered products. As long as there are large amounts of medicines and companies, doctors and uninformed patients, marketing will remain as is. As for their impact, they do not have any impact. The price is defined on the basis of the 80% rule.

- **What do you think of generic substitutes and giving the pharmacist the full authority to replace the medicine without referring to the doctor?**

In this case, the pharmacist will negotiate with companies to get the largest possible bonus. Such medicines are then replaced just for the benefit of the pharmacist and not to serve the interest of the patient.

- **What do you think of writing the prescription by using the scientific name rather than the trade name of a medicine?**

Not in the interest of the patient. The pharmacist will replace the medicine that brings him the highest profit gained by the bonus. The public sector and in-hospital patients may benefit from that.

To sum up, the issue of medicine in Jordan can be sorted out as follows:

1- New applicable good pricing rules
2- JFDA should work for the interest of people rather than for the interest of companies and factories. I told you, the rules were laid down but they were not approved by the higher committee that comprised members of close relations with Jordan pharmaceutical companies. Some of them are even incorporators or shareholders.
3- Pharmacists should improve their performance by introducing the technical fees' rule.
4- Pharmacists' Association should play a better role.

Appendix 7

Kingston University London

حزيران 2012

تحية طيبة وبعد ،،،

يرجى العلم بأن أول دواء يتم إنتاجه لعلاج المرض يسمى الدواء الأصيل، بعد سنوات قليلة تستطيع الشركات الأخرى أن تنتج دواء مماثل بنفس المادة الطبية الفعالة وهو ما يسمى الدواء الجنيس.الدواء الجنيس يكون قابل للتبديل مع الدواء الأصيل لأن كلا منهما يعمل بنفس الطريقه العلاجيه في جسم الانسان.على سبيل المثال: بانادول® هي علامة تجارية لدواء أصيل بينما ريفاتين® هي علامة تجارية لدواء جنيس مصنع محليا وكلاهما يحتوي على نفس الماده الطبية الفعالة (باراسيتامول).

تعتبر الأدوية الجنيسة مكافئة للأدوية الأصيلة من حيث الجرعة والشكل الصيدلاني، الأمان، التركيز، الفعالية، الجودة، طريقة التعاطي وادواعي الاستعمال. وعادة ما يتم إنتاجها بعد سقوط براءة الإختراع أو الحماية الفكرية عن الدواء الأصيل.

هذا الاستبيان يهدف إلى دراسة معتقدات المرضى فيما يتعلق بالأدوية الجنيسة، واستبدال الأدوية الأصيلة بالجنيسة وأسعار الأدوية في الأردن. وهو جزء من اطروحة الدكتوراه بالصيدلة من جامعة كنجستون – لندن – بريطانيا.

لم تجرى دراسات كافية في الأردن لتقييم تصورات المرضى عن الأدوية الجنيسة في الأردن. على الرغم من أن ذلك أمر ضروري لوضع سياسة سليمة للأدوية الجنيسة في الأردن و تسعيرها.

علماً بأن هذه الدراسة قد تمت الموافقة عليها من قبل لجنة أخلاقيات البحث العلمي في جامعة كينغستون. إن إجاباتكم هامة جدا لإستكمال البحث بدقة مع ملاحظة أن كافة الإجابات ستبقى سريه في كافة مراحل هذه الدراسة، ولن يتم استخدامها في غير نطاق البحث العلمي.

سيكون الباحث ممتنا لو تمت الإجابة عن هذه الأسئلة بكل أمانه وصدق وموضوعية. إذا كنتم بحاجة إلى مزيد من المعلومات حول هذه الدراسة، لا تترددوا في الاتصال مع الباحث من خلال البريد الالكتروني أو الهاتف أدناه:

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Appendix 8

معتقدات المرضى فيما يتعلق بالأدوية الجنيسة، وإستبدال الأدوية الأصيلة بالجنيسة وأسعار الأدوية في الأردن

يرجى قراءة الفقرة التالية بتمعن قبل البدء باجابة الإستبيان:
" أول دواء يتم انتاجه لعلاج المرض يسمى الدواء الأصيل، بعد سنوات قليلة الشركات الأخرى تستطيع أن تنتج دواء مماثل بنفس المادة الطبية الفعالة وهو ما يسمى الدواء الجنيس. الدواء الجنيس يمكن أن يكون قابل للتبديل مع الدواء الأصيل لأن كلا منهما يعمل بنفس الطريقة العلاجية في جسم الانسان. على سبيل المثال: باتادول® هي علامة تجارية لدواء أصيل بينما ريفاتين® هي علامة تجارية لدواء جنيس مصنع محليا و كلاهما يحتوي على نفس الماده الطبية الفعالة (باراسيتامول)."

الجزء أ: المعتقدات و الاستعمالات للأدويه الجنيسه عند المرضى في الأردن.

* الرجاء الاجابه بوضع اشارة (X) في المربع المناسب لكل عباره ممايلي:

رقم السؤال	العبارات	أوافق بشدة	أوافق	لا أوافق	لا أوافق بشده
1	يجب على الأطباء سؤال مرضاهم عن أدويتهم المفضلة.				
2	يجب أن يكون هناك خيار للمرضى في الإختيار بين الدواء الجنيس و الدواء الأصيل.				
3	أنا لا أمانع اذا إستبدل الصيدلاني الدواء الموصوف لي بأرخص دواء مماثل له				
4	أنا لا أمانع إستبدال الدواء الموصوف لي من دواء أصيل الى دواء جنيس (مثال استبدال الباتادول بالريفاتين)				
5	الحالة الوحيده لاستبدال الدواء الموصوف لي من دواء اصيل الى دواء جنيس بديل هي بناءا على طلبي فقط. (مثال استبدال الباتادول بالريفاتين)				
6	أنا لا أمانع اذا استبدل الصيدلاني الدواء الموصوف لي بالبديل المحلي المماثل و المطابق.				
7	انا افضل ان توصف لي الأدوية المحلية.				
8	أنا افضل ان توصف لي الادوية التي علامتها التجارية مشهورة.				
9	أنا افضل ان توصف لي الأدوية المستوردة بدلا من الأدوية المحلية.				
10	تكلفة الدواء يجب ان تؤخذ بعين الاعتبار قبل أن يوصف.				
11	انا لا أهتم اذ كان دوائي الموصوف / المصروف محليا او مستوردا طالما كان الدواء فعالا.				
12	أنا أفضل ان يوصف لي / يصرف لي الدواء الأرخص المتوفر لعلاج حالتي.				
13	التكلفة ليست مهمه لي طالما الدواء سيعالج حالتي.				
14	الدواء الأغلى سعرا هو الأفضل.				
15	الأدويه المستوردة هي الأفضل.				
16	استعمال الأدوية الجنيسة سيحقق توفيرا كبيرا بالنسبة لي.				
17	بشكل عام تكلفة الدواء في الأردن مرتفعة جدا.				

الجزء ب: المعلومات الديموغرافية.

مستوى دخل الاسره: ☐اقل من 250 دينار ☐250-500 دينار ☐ 501-750 دينار
☐751- 1000 دينار ☐ اكثر من 1000 دينار

المستوى التعليمي: ☐ دراسات عليا ☐ بكالوريوس ☐ كلية مجتمع ☐ ثانويه فما دون

نسبة التحمل من تكلفه الدواء: ☐ ادفع كامل سعر الدواء ☐لا ادفع على الاطلاق ☐ ادفع نسبه مئويه محددة من التكلفة

عدد الأدويه في وصفتك: ☐1-3 ☐ 4-6 ☐ اكثر من 6

الحاله المرضيه المزمنه: ☐ أمراض الجهاز التنفسي(ربو) ☐ أمراض القلب (ضغط) ☐ أمراض الغدد الصماء (سكري)
☐أخرى الرجاء التحديد ----------

الحاله الصحيه العامه: ☐ ممتازة ☐ سيئه ☐ وسط ☐ جيدة ☐ جيدة جدا

تجاوبك محل تقدير كبير
شكرا جزيلا لك على المشارك

Appendix 9

Kingston University London

May 2012

Dear Sir/Madam,

I am kindly requesting your participation in this survey, which aims to investigating patients' perceptions of generic medicines, generic substitution and prices of medicines in Jordan. This study is part of my pharmacy PhD project.

The first medicine comes to treat a disease is called an **originator** medicine, a few years after other companies can produce a similar medicine with the same active ingredient which is called a **generic** medicine. A generic medicine can be interchangeable with the originator medicine as both acts in the same way in the human body. This process is called generic substation. For example: Panadol® is the originator brand while Revanin® is the generic one which is produced locally, and both of them contain the same active ingredient (Paracetamol)."

The use of generic medicines is widely encouraged by most governments across the world as a cost-containment strategy to both the healthcare system and the patients. However, insufficient studies have been conducted in Jordan to evaluate patients' perceptions of generic medicines in Jordan. Therefore, understanding perceptions held to these issues are very important in establishing a sound generic medicine policy in Jordan.

This study has been approved by the Kingston University Ethics Committee. Please note confidentiality will be maintained at all times and no individuals will be identifiable in the results of this study.

I will be grateful if you can take 5 minutes to complete the questionnaire and return it to me by hand. If you need any further information regarding this study, do not hesitate to contact me.

My details are:

Email address: K0740390@kingston.ac.uk

My Supervisor email: r.kayyali@kingston.ac.uk

My mobile: +447964528599 (UK), 0777713688 (Jordan)

Thank you in advance for your appreciated help.

Yours sincerely

Faris El-Dahiyat

Appendix 10

Perceptions of patients' towards generic medicines, generic substitution and medicines price in Jordan.

Please read the following statement:

"The first medicine comes to treat a disease is called an **originator** medicine, a few years after other companies can produce a similar medicine with the same active ingredient which is called a **generic** medicine. A generic medicine can be interchangeable with the originator medicine as both acts in the same way in the human body. For example: Panadol® is the originator brand while Revanin® is the generic one which is produced locally, and both of them contain the same active ingredient (Paracetamol)."

Part A: generic perception and use among patients in Jordan.

* For each of the statement, please mark your response by a tick (√) **in the appropriate box.**

Question No	Statements	Strongly Agree	Agree	Disagree	Strongly Disagree
1	Physicians should ask patients about their medicines preference.				
2	Patients should have the option of choosing between generic and originator.				
3	I don't mind the pharmacist substituting the medicine I was prescribed to a cheaper equivalent one.				
4	I don't mind my prescribed medicines to be substituted from originator to generic. (e.g. Panadol to Revanin)				
5	My medicines should only be substituted from originator to generic if I request. (e.g. Panadol to Revanin)				
6	I don't mind the pharmacist substituting my prescribed medicine to an equivalent locally produced one.				
7	I prefer to be prescribed locally produced medicines.				
8	I prefer to be prescribed a well-known brand.				
9	I prefer to be prescribed imported rather than local medicines.				
10	Costs should be considered before a drug is prescribed.				
11	I don't mind whether my prescribed / dispensed medicine is locally produced or imported as long as it is effective.				
12	I prefer to be prescribed / dispensed the cheapest medicine available for the treatment of my condition.				
13	Cost is not an issue for me as long as the medicine will treat my condition.				
14	A more expensive medicine is a better one.				
15	Imported medicines are better.				
16	Using generic medicines would provide significant saving to me.				
17	In general, medicine costs in Jordan are too high.				

Part B : Demographic Questions

1- The monthly income: ❑less than 250 ❑250-500JD ❑501-750JD ❑751-1000JD ❑more than 1001 JD

2- Educational level: ❑Post graduate ❑bachelor degree ❑College ❑High school

3- Cost of medicine? ❑pay full cost ❑pay percentage ❑do not pay at all

4- Number of drugs in your prescriptions: ❑ 1-3 ❑4-6 ❑more than 6

5- Medical Condition: ❑Cardiovascular ❑Diabetics ❑respiratory disease ❑Other, specify----------

6- General health status: ❑excellent ❑ very good ❑ good ❑fair ❑poor

Is there any additional information that you would like to provide regarding the topic of this questionnaire?

Your response is very much appreciated.
Thank you for participating!

Appendix 11

Kingston University London

May 2012

Dear Pharmacist,

I am kindly requesting your participation in this survey, which aims to investigate Jordanian community pharmacists' perception about generic substitution, current practices and opinions about future implementation of generic substitution law. This study is a part of my pharmacy PhD project.

The use of generic medicines is widely encouraged by most governments across the world as a cost-containment strategy to both the healthcare system and the patients. However, the concept of generic prescribing and dispensing has been controversial and questions remain regarding the eventual diffusion of generic practices among some medical practitioners. These controversies surround issue such as quality, safety and efficacy of generic medicines.

Currently, insufficient studies have been conducted in Jordan to evaluate the Pharmacists' perception and current practice of generic substitution. Therefore, understanding perceptions held to these issues are very important in establishing a sound generic medicine policy in Jordan.

This study has been approved by the Kingston University Ethics Committee. Please note confidentiality will be maintained at all times and no individuals will be identifiable in the results of this study.

I am enclosing a copy of the questionnaire for you to complete if you wish to participate. I will come to collect the completed questionnaire in one week time. If you need any further information about this study, do not hesitate to contact me. My details are:

My details are:

Email address: K0740390@kingston.ac.uk

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Thank you in advance for your appreciated help.

Yours sincerely

Faris El-Dahiyat

Appendix 12

Generic substitution perception and practice among community pharmacists in Jordan.

Part A: Perception on generic substitution.

1- Please indicate which statement best expresses your general opinion regarding generic substitution? (please choose one)

- ❑ I support generic substitution in all cases where a generic is available.
- ❑ I support generic substitution in most cases, but there are some situations where it is not appropriate.
- ❑ I do not support generic substitution.

2- Generic substitution is suitable for? ?(please choose as many options as applicable)

- ❑ Over-the-counter medicine.
- ❑ Prescription only medicine.

* For each of the statement, please mark your response by a tick (√) **in the appropriate box.**

Question No	Statements	Strongly Agree	Agree	Disagree	Strongly Disagree
3	A generic medicine is bioequivalent to its originator.				
4	The quality of originator medicines is better compared to generics.				
5	Generic medicines are less effective compared to originators.				
6	Generic medicines are cheaper alternatives to originators.				
7	The prices of medicines in Jordan relatively reflect the income per capita.				

Part B: Current generic substitution.

1- In your current practice, how often do you consult the physician when performing generic substitution?(please choose one)

- ❑ Never, please proceed to question 2 below.
- ❑ Rarely, please proceed to question 2 below.
- ❑ Sometimes, please proceed to question 2 below.
- ❑ Frequently, please proceed to question 2 below.
- ❑ Always, please proceed to question 3 below.

2- Please tell us your reason(s) for not consulting the physician when performing generic substitution?(please choose as many options as applicable)

- ❑ The drugs involved are non-prescription items which do not require consultation with the prescribing physician.
- ❑ Do not have the contact numbers of the physician.
- ❑ Too busy.
- ❑ No confidence to communicate with the physician.
- ❑ Do not think it is necessary to consult the physician.
- ❑ Other, please specify ----------

3- What types of information do you consider or provide to the physician when performing generic substitution? ?(please choose as many options as applicable)

- ❑ Reasons for generic substitution.
- ❑ Choices of generic medicines.
- ❑ Prices of generic medicines.
- ❑ How much is the cost-saving.
- ❑ Quality of the generic drugs.
- ❑ Patient's satisfaction with the generic drugs.
- ❑ Your own experiences with the generic drugs.
- ❑ Other, please specify ----------

4- What type of information do you provide to the patient when performing generic substitution?(please choose as many options as applicable)

- ❑ Reasons for generic substitution.
- ❑ Choices of generic drugs.
- ❑ Prices of generic drugs.
- ❑ How much is the cost-saving.
- ❑ Quality of the generic drugs.
- ❑ Physician's satisfaction with the generic drugs.
- ❑ Your own experiences with the generic drugs.
- ❑ Others, please specify ----------

5- Have you observed any of the following problems when a patient switched from originator brand to generic? (please choose as many options as applicable)

- ❑ Patient has reported no therapeutic effect.
- ❑ Patient developed an allergic reaction.
- ❑ Product returned as patient thought it was the wrong one.
- ❑ Patient demanded the originator brand version.
- ❑ Patient reported increase in side effect.
- ❑ Other, please specify ----------.

Part C: Future implementation of generic substitution policy.

1- Which of the following standard of practice do you prefer? (please choose one)

- ❑ Pharmacists are allowed to perform generic substitution without consulting the prescribing physician.
- ❑ Pharmacists must consult the prescribing physician when performing generic substitution.
- ❑ Pharmacists are only required to consult the prescribing physician when substituting certain group of drugs.

2- Which group of drugs do you prefer to consult the prescribing physician when performing generic substitution for? (please choose as many options as applicable)

- ❑ Over-the-counter medicine.
- ❑ Prescription only medicine.
- ❑ Controlled drug.
- ❑Narrow therapeutic Index Drugs.

3- Generic substitution should occur: ?(please choose as many options as applicable)

- ❑ At the request of physicians.
- ❑ At the request of patient.
- ❑ On the pharmacist judgment.

Question No	Statements	Strongly Agree	Agree	Disagree	Strongly Disagree
4	Community pharmacists in Jordan should be given generic substitution right.				
5	Generic substitution should be allowed only at patient request.				
6	A prescribing system based on the international non-proprietary name INN should be implemented.				
7	Prescribers should write prescription using the international non-proprietary name INN, and pharmacists be allowed to dispense any brand against a prescription.				
8	Pharmacy profit margin should be variable according to your professional decision.				
9	Quality use of generic medicines among Jordanian consumers can be achieved if both physicians and pharmacist work together.				
10	Pharmacist should always dispense the the originator prescribed.				

11- Pharmacy medicine profit margin should be: (please choose one)

- ❑ Increased.
- ❑ Decreased.
- ❑ Remain as it is.

12- If generic substitution by pharmacist become allowed , profit margin should be: (please choose one)

- ❑ Increased.
- ❑ Decreased.
- ❑ Remain as it is.

13- If generic substitution by pharmacist become allowed, the following measures needs to be adopted ?(please choose as many options as applicable)

- ❑ Locally produced generic medicine needs to be provided.
- ❑ The cheapest generic medicine needs to be provided.
- ❑ the generic of patient choice need to be provided
- ❑ A clear pricing list of equivalent originator/generic medicines needs to be in each pharmacy to be provided to patient upon request.
- ❑ A clear pricing list of equivalent originator/generic medicines needs to be in each pharmacy to be used by pharmacists to support decision making.
- ❑ Other, please specify----------.

Part D: Demographic Questions.

1- Gender: Male ❑ Female ❑

2- Age (in years): Under 30 ❑ 30-40 ❑ 41-50 ❑ 51-60 ❑ above 60 ❑

3- Practicing years: 1 -5 ❑ 6-10 ❑ 11-15 ❑ 16-20 ❑ 21 and above ❑

4- Employment Position: Self or part owner ❑ Employee ❑

5- Location of the pharmacy: West Amman ❑ East Amman ❑

Is there any additional information that you would like to provide regarding the topic of this questionnaire?

Your response is very much appreciated.
Thank you for participating!

Appendix 13

Kingston University London

25th April 2012

Dear Doctor,

I am kindly requesting your participation in this survey, which aims to investigate prescribing behaviour, perception and issues regarding the use of generic medicines of Jordanian physicians. This study is a part of my pharmacy PhD project.

The use of generic medicines is widely encouraged by most governments across the world as a cost-containment strategy to both the healthcare system and the patients. However, the concept of generic prescribing and dispensing has been controversial and questions remain regarding the eventual diffusion of generic practices among some medical practitioners. These controversies surround issues such as quality, safety and efficacy of generic medicines.

Currently, insufficient studies have been conducted in Jordan to evaluate the knowledge and perceptions of physicians with regard to generic medicines and generic prescribing. Therefore, understanding perceptions held to these issues are very important in establishing a sound generic medicine policy in Jordan.

This study has been approved by the Kingston University Ethics Committee. Please note that confidentiality will be maintained at all times and no individuals will be identifiable in the results of this study.

I am enclosing a copy of the questionnaire for you to complete if you wish to participate. I will come to collect the completed questionnaire in one week time. If you need any further information about this study, do not hesitate to contact me. My details are:

Email address: K0740390@kingston.ac.uk

My Supervisor email: r.kayyali@kingston.ac.uk

My mobile: +447964528599 (UK), 0777713688 (Jordan)

Thank you in advance for your appreciated help.

Yours sincerely

Faris El-Dahiyat

Appendix 14

A survey on the prescribing behavior, perceptions of physicians towards generic medicines and issues pertaining the use of generics in Jordan.

Part A: Prescribing behavior.

1- Rank the following factors that may influence your decision when prescribing a medicine. (1= most important, 6=least important)

- ____ The clinical effectiveness and safety of a drug.
- ____ Pharmaceutical dosage form and daily recommended dose.
- ____ Patient preference.
- ____ Cost to the patient.
- ____ Availability as generic.
- ____Country of origin.

2- What sources do you consider for justifying your prescribing decision? (please choose as many options as applicable)

- ❑ Local guidelines and local protocols.
- ❑ Medical journals publication and online database.
- ❑ Conferences.
- ❑ Pharmaceutical sales representative.
- ❑ International treatment guidelines.
- ❑ Others, please specify ----------

3- The cost of a drug in your prescribing decision is: (please choose one)

- ❑ Highly important.
- ❑ Important.
- ❑ Not very important.
- ❑ Not at all important.

4- What sources do you take into account when searching for information about cost of drugs? (please choose as many options as applicable)

- ❑ Jordan food and drug administration (JFDA) website.
- ❑ Pharmacists.
- ❑ Pharmaceutical sales representative.
- ❑ Others, please specify ----------

5- How often do you prescribe generic medicine instead of originator brand? (please choose one)

- ❑ Very often.
- ❑ Often.
- ❑ Rarely.
- ❑ Hardly ever.

6- How often do you write prescriptions using the International Non-priority Name (INN)? (please choose one)

- ❑ Very often.
- ❑ Often.
- ❑ Rarely.
- ❑ Hardly ever.

Part B: Perceptions about generics.

* For each of the statement, please mark your response by a tick (√) **in the appropriate box.**

Question No	Statements	Strongly Agree	Agree	Disagree	Strongly Disagree
1	Generic substitution offer significant cost advantage to the patient.				
2	Generic substitution will allow pharmacists to select to select the most affordable drug to a patient.				
3	Ability to perform generic substitution will ensure prompt availability of medications to the patient				
4	Generic substitutions will increase the use of locally produced medicines.				

Part C: Generic medicine utilisation and substitution in Jordan.

Question No	Statements	Strongly Agree	Agree	Disagree	Strongly Disagree
1	It is feasible to implement prescribing system based on International Non-priority Name (INN).				
2	Standard guidelines on generic substitution process to both physicians and pharmacists should be implemented.				
3	Implementing an electronic prescription service would result in a more efficient prescribing and dispensing process.				
4	Generic substitution should be allowed only at patient request.				
5	Quality use of generic medicines among Jordanian consumers can be achieved if both physicians and pharmacist work together.				
6	Developing a computerized system which includes important information about drugs such as: medicines interaction, contraindications and cost, would improve the prescribing process				
7	Community Pharmacist in Jordan should be given generic substitution right.				

8- Please indicate which statement best expresses your general opinion regarding generic substitution by community pharmacists? (please choose one)

- ❑ I accept generic substitution for brand name medicines in all cases where a generic is available, proceed to question 8
- ❑ I accept generic substitution for brand name medicines in most cases, but there are some situations where it is not appropriate, (e.g narrow therapeutic index medicines Digoxin, Carbamazepine, warfarin).Proceed to question 9
- ❑ I do not accept generic substitution for brand name medicine by pharmacists, proceed to part D.

9- Which of the following standard of practice do you prefer? (please choose one)

- ❑ Pharmacists are allowed to perform generic substitution without consulting the prescribing physician.
- ❑ Pharmacists must consult the prescribing physician when performing generic substitution.
- ❑ Pharmacists only required to consult the prescribing physician when substituting certain group of drugs.

Part D: Demographic Questions.

1- Gender: Male ❑ Female ❑

2- Age (in years): Under 30 ❑ 30-40 ❑ 41-50 ❑ 51-60 ❑ above 60 ❑

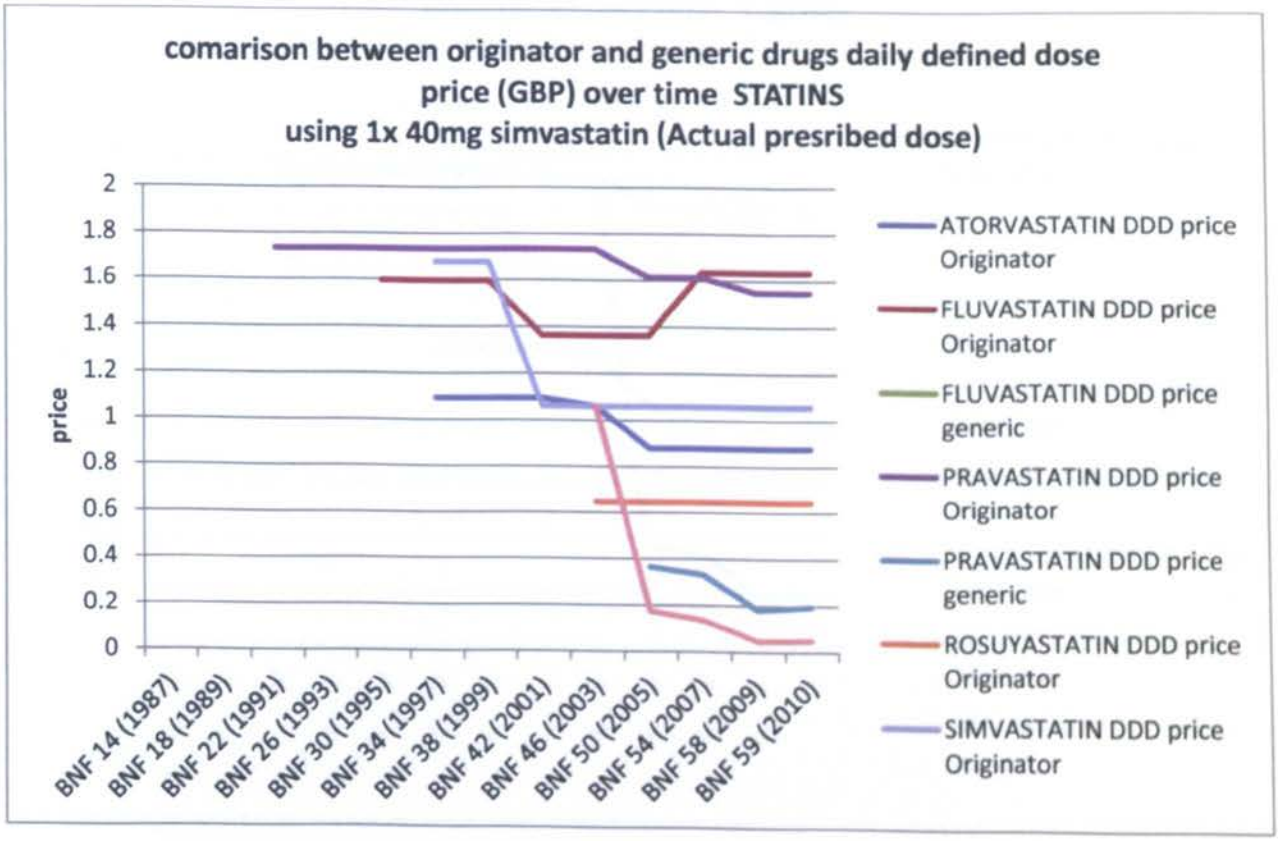
3- Practicing years: 1 -5 ❑ 6-10 ❑ 11-15 ❑ 16-20 ❑ 21 and above ❑

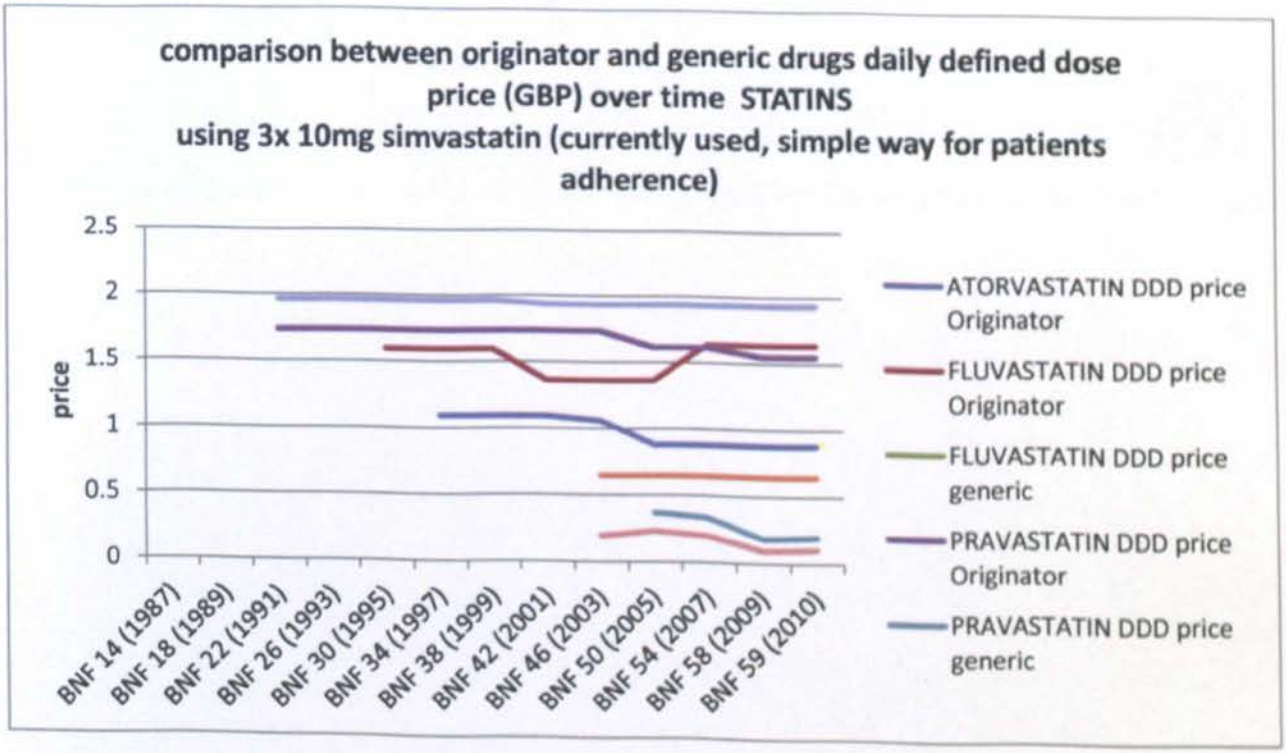
4- Employment sector: private ❑ public ❑

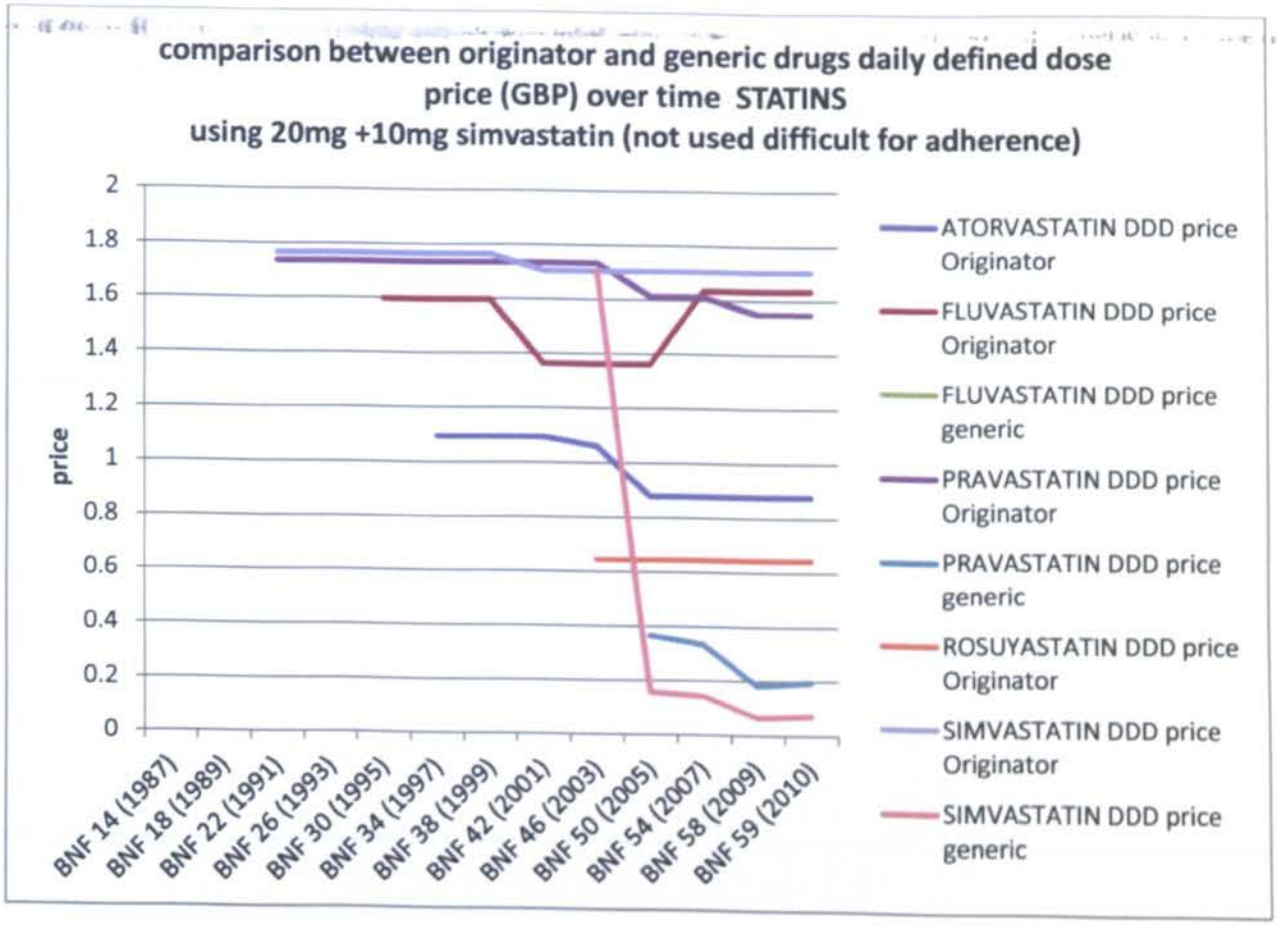
Is there any additional information that you would like to provide regarding the topic of this questionnaire?

Your response is very much appreciated.
Thank you for participating!

Appendix 15


comarison between originator and generic drugs daily defined dose price (GBP) over time STATINS using 1x 40mg simvastatin (Actual presribed dose)
price
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
BNF 14 (1987)
BNF 18 (1989)
BNF 22 (1991)
BNF 26 (1993)
BNF 30 (1995)
BNF 34 (1997)
BNF 38 (1999)
BNF 42 (2001)
BNF 46 (2003)
BNF 50 (2005)
BNF 54 (2007)
BNF 58 (2009)
BNF 59 (2010)
ATORVASTATIN DDD price Originator
FLUVASTATIN DDD price Originator
FLUVASTATIN DDD price generic
PRAVASTATIN DDD price Originator
PRAVASTATIN DDD price generic
ROSUYASTATIN DDD price Originator
SIMVASTATIN DDD price Originator


comparison between originator and generic drugs daily defined dose price (GBP) over time STATINS using 3x 10mg simvastatin (currently used, simple way for patients adherence)
price
2.5
2
1.5
1
0.5
0
BNF 14 (1987)
BNF 18 (1989)
BNF 22 (1991)
BNF 26 (1993)
BNF 30 (1995)
BNF 34 (1997)
BNF 38 (1999)
BNF 42 (2001)
BNF 46 (2003)
BNF 50 (2005)
BNF 54 (2007)
BNF 58 (2009)
BNF 59 (2010)
ATORVASTATIN DDD price Originator
FLUVASTATIN DDD price Originator
FLUVASTATIN DDD price generic
PRAVASTATIN DDD price Originator
PRAVASTATIN DDD price generic


comparison between originator and generic drugs daily defined dose price (GBP) over time STATINS
using 20mg +10mg simvastatin (not used difficult for adherence)
price
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
BNF 14 (1987)
BNF 18 (1989)
BNF 22 (1991)
BNF 26 (1993)
BNF 30 (1995)
BNF 34 (1997)
BNF 38 (1999)
BNF 42 (2001)
BNF 46 (2003)
BNF 50 (2005)
BNF 54 (2007)
BNF 58 (2009)
BNF 59 (2010)
ATORVASTATIN DDD price Originator
FLUVASTATIN DDD price Originator
FLUVASTATIN DDD price generic
PRAVASTATIN DDD price Originator
PRAVASTATIN DDD price generic
ROSUYASTATIN DDD price Originator
SIMVASTATIN DDD price Originator
SIMVASTATIN DDD price generic

PUBLICATIONS

Original paper

Generic Medicines

Journal of Generic Medicines
0(0) 1–8

DOI: 10.1177/1741134313502978
jgm.sagepub.com
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Community pharmacists' perceptions towards generic medicines and their opinions on future generic substitution policy implementation: A descriptive study from Jordan

Faris Abdelrahim El-Dahiyat and Reem Kayyali

Abstract

The aim of this study was to explore Jordanian pharmacists' perceptions towards generic medicines as well as to evaluate their opinions on generic substitution in order to introduce a future generic substitution policy in Jordan. A cross-sectional descriptive study involving community pharmacists in Amman-Jordan was undertaken, using a self-completed anonymous questionnaire. The sampling unit was community pharmacy, and the sampling frame was list of community pharmacies in Amman (N = 1252). Five hundred pharmacies were randomly selected to participate in this survey, and 294 pharmacists' responses were collected giving a response rate of 58.8%. The majority of Jordanian pharmacists had a positive view on generic medicines in general with 87.7% of the respondents believing that a generic medicine is bio-equivalents to the originator. Two hundred and sixty-five pharmacists (90.1%) were in favour of implementing a compulsory generic prescribing policy. More than 80% of the pharmacists supported generic substitution in most cases. Generic substitution policy should be implemented; in addition, a formulary of interchangeable medicines must be developed to guide pharmacists' decision making when performing generic substitution. Jordanian pharmacists were also in favour of introducing a compulsory generic prescribing legislation; however, such policy may have a negative impact on the local industry, as most of the produced medicines are branded generics.

Keywords

Generic medicines, generic substitution, community pharmacist, perception, policy

Introduction

The high health care expenditure on pharmaceutical products is becoming a challenging issue worldwide. The use of cheaper generic medicines helps tackle this issue by providing savings to patients as well as governments.[1,2] A generic medicine is defined as a medicinal product, which is identical in the active ingredient qualitative and quantitative composition, and whose bioequivalence has been established with an originator medicine, whose granted patent protection has expired.[3,4]

Generics promote price competition that reduces price through a cost-effective way since generics are alternatives to higher priced originator pharmaceuticals.[5,6] Generic medicines not only provide the same quality, safety and efficacy when compared to originator medicines,[7] but also generally they are 20–90% less expensive than the innovator medicines.[1] It has been estimated that €25 billion is the annual save made by European patients and health care systems for using generic medicines.[1] Public and private third-party payers and healthcare authorities therefore increasingly encourage or mandate the use of generics through measures such as generic prescribing and generic substitution.[7,8]

Generic substitution is the practice of switching from a prescribed originator medicine to an

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interchangeable generic medicine at the time of dispensing.[9]

In the United States, once a generic medicine has been approved by the Food and Drug Administration, this medicine can be dispensed by pharmacists as a substitute to its reference prescribed originator medicine, taking into consideration the generic medicine has the same clinical efficacy as well as safety.[10]

In 2003, pharmacists in Finland were obligated to switch a prescribed medicine to the least or close to least expensive medicine (usually the generic equivalent), provided that the prescribed medicine is not within certain defined limit (price corridor) of the maximum price, and neither the prescriber nor the patient objects the substitution. The price corridor is reviewed every 3 months on the basis of price notifications submitted by pharmaceutical companies.[11,12] The total savings generated during the first year of implementation amounted to 88.3 million euro.[13]

In UK, it was reported that more than 83% of the prescriptions in 2007 were written generically,[14] thus making the issue of generic substitution less pressing. In addition, pharmacists have an economic incentive, through supplier discounts, to dispense generic medicines.[15] In England, 68.9% of all prescription items were dispensed as generic medicines in 2011.[16]

In Canada, the IMS Health reports showed that 54% of all prescriptions were dispensed using generic medicines in the year 2009. This made a saving of $4 billion to Canada's health care system. Higher figures were reported in the United States; according to IMS Health reports, generic medicines were dispensed to fill 75% of all prescriptions in USA.[17]

In Jordan, a circular from the Ministry of Health required doctors in Government hospitals and health clinics to prescribe generically. However, if a brand name is prescribed, the patient gets the formulary drug anyway, unless their physician builds a case and receives special permission to have the brand name dispensed. Furthermore, private health insurance companies encourage doctors to prescribe the lowest priced generic.[18] On the other hand, in the private sector, there is no requirement or encouragement to prescribe generics.

Under the current Jordanian legislation, pharmacists are not permitted to make any change or substitution to prescriptions,[19] unless the pharmacist contacts the prescriber and requests permission for the prescribed originator medicine to be substituted by an alternative generic medicine.

In Jordan, all pharmaceutical prices include the same mark-up percentage (fixed profit margin), and wholesaler receives 15% profit on the landed cost plus 4% for expenses while pharmacy receives 20% profit on the wholesale price plus 6% expenses. In addition, there is a value-added tax of 4%. These percentages are cumulative.[20]

This implies that there is no financial incentive for the generics to be prescribed or dispensed, since originator and generic medicines have the same % mark-up profit.[21] This is why it is more profitable to sell the highest priced originator medicines as this attracts the highest return in money terms.[22]

This study aims to assess the perceptions held by community pharmacists in Jordan regarding generic medicines, their current generic substitution practice and their opinion on future implementation of generic substitution. Due to the lack of previous studies regarding generic substitution in Jordan, the findings from this study would provide a baseline data for establishing a robust generic medicine policy in Jordan.

Methods

This is a cross-sectional study whereby a questionnaire was used to collect data from Jordanian pharmacists working in community pharmacies in both affluent and deprived areas of Amman. This study was adapted from previous studies held in the same area of interest, which were identified through literature search.[23]

The questionnaire was tested for face and content validity by two experts. It was further revised after pilot testing with 10 community pharmacists. There are four sections in the questionnaire. The first section evaluated the knowledge about generic medicines and the perceptions regarding originator to generic substitution among the surveyed community pharmacists. The second section explored pharmacists' current generic substitution practice. The third section explored pharmacists' views of future implementation of generic substitution policy. The last section characterised the respondent demographics.

The responses were framed in different types such as single answer and multiple answer closed questions and four-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) questions.

In this study, the population was identified as Jordanian registered community pharmacists. The sampling unit was community pharmacy, and the sampling frame was list of community pharmacies in Amman (N = 1252), which was obtained from the Jordanian Pharmaceutical Association. A representative sample of 294 was calculated from the population (N = 1252) with 5% margin of error and 95% confidence level. In order to reach the representative sample size of 294, 500 pharmacies were randomly selected to participate in this survey by using Microsoft Excel randomization software.[24]

Invitation letters along with the questionnaire were given to each pharmacy, and the questionnaires were collected within a week time. When the representative sample size (294 questionnaires) was reached, data collection stopped (response rate was 58.8%).

The participation of pharmacists approached was strictly voluntary, and their informed consent was obtained. Anonymity of respondents was preserved in the study, as names of participants were not included.

Data were collected from 15 June 2012 to 15 July 2012. All the collected data were entered into PASW® 18.0 for descriptive analysis using descriptive statistics techniques such as frequency and cross-tabulation and inferential statistics using chi square tests.

This study was approved by the Research Ethics Committee of Kingston University, London. Participation was voluntary and anonymous.

Results

Demographic characteristics of responding pharmacists

A total of 294 responses were received, and the basic demographic of the responding pharmacists is summarised in Table 1. The sample was almost equally distributed between males (142, 48.3%) and females (152, 51.7%). The modal age of the responding pharmacists was under 30 years with a range of under 30–60. Respondents mostly had 1–5 years' experience in practicing pharmacy. Regarding the employment position, the majority of respondents were employees; almost the same number of responses were collected from pharmacists working in the affluent area in Amman (West) and the deprived area of Amman (East) (Table 1).

Table 1. Demographics and practice characteristics.

Characteristic	*N* (%)
Gender	
Male	142 (48.3)
Female	152 (51.7)
Age group (years)	
Under 30	159 (54.1)
30–40	100 (34.0)
41–50	24 (8.2)
51–60	11 (3.7)
Above 60	0 (0.0)
Practicing (years)	
1–5	167 (56.8)
6–10	35 (11.9)
11–15	60 (20.4)
16–20	17 (5.8)
21 and above	15 (5.1)
Employment position	
Self or part owner	75 (25.5)
Employee	219 (74.5)
Location of the pharmacy	
West Amman (affluent)	160 (54.4)
East Amman (deprived)	134 (45.6)

Knowledge of generics and perception of generics' substitution and prices of medicines

When assessing the pharmacists' views on generic medicines, the pharmacists predominantly agreed that a generic medicine is bioequivalent to its originator (87.7%, n = 258). Most of the respondents (61.9%, n = 182) disagreed that the quality of originator medicine is better compared to generics. About 59.8% of the pharmacists disagreed that the generic medicines are less effective compared to originators (n = 176). The vast majority of respondents agreed that the generic medicines are cheaper alternative to the originators (90.2%, n = 265). Further analysis found that 55.4% of the pharmacists perceived that the prices of medicine in Jordan do not relatively reflect the income per capita (n = 163) (Table 2).

The pharmacists' opinions were further evaluated on generic substitution, and more than half of the respondents (56.8%, n = 167) supported generic substitution in most cases, while 23.8% supported the substitution in all cases where a generic is available (n = 70), and the rest did not support generic substitution (19.4%, n = 57) (Figure 1).

The pharmacists were asked about the type of medicines, which is suitable for generic substitution, 78.2% of them believed that generic substitution is suitable for over-the-counter medicine (OTC), whereas 69.4% agreed to generic substitution for prescription-only medicine (POM) (Figure 2).

Perception of future implementation of generic substitution policy

When pharmacists were asked about their preference regarding the implementation of future generic substitution policy, 41.2% responders believed that they only need to consult the physician when substituting certain groups of medicines (n = 121). However, 30.6% of responders preferred to perform generic substitution without consulting the prescriber physician (n = 90). Only 28.2% (n = 83) of the pharmacists believed that they must always consult the physician when performing generic substitution.

Table 2. Community pharmacists' responses to four-point Likert scale questions exploring knowledge of generics and perception of generics' substitution and prices of medicines.

Question	Survey questions/statement	Frequency (%)			
		Strongly disagree	Disagree	Agree	Strongly agree
1	A generic medicine is bioequivalent to its originator.	15 (5.1)	21 (7.1)	202 (68.7)	56 (19)
2	The quality of originator medicines is better compared to generics.	73 (24.8)	109 (37.1)	97 (33)	15 (5.1)
3	Generic medicines are less effective compared to originators.	28 (9.5)	148 (50.3)	111 (37.8)	7 (2.4)
4	Generic medicines are cheaper alternatives to originators.	3 (1)	26 (8.8)	221 (75.2)	44 (15)
5	The prices of medicines in Jordan relatively reflect the income per capita.	70 (23.8)	93 (31.6)	100 (34)	31 (10.5)

Further analysis showed the types of medicines that need consultation with the physician when performing generic substitution. The majority of pharmacists (69%, n = 203) preferred to consult the physician when substituting narrow therapeutic index drugs and 58.5% of the pharmacists preferred to consult when substituting controlled drug (n = 172). Regarding POM, only 38.1% of the responders felt that they need to consult a physician when substituting these drugs (n = 112), whereas only 15.3% (n = 45) of responders preferred to consult a physician when performing generic substitution for OTC drug medicines.

Two-thirds (68.4%, n = 201) of the pharmacists, who answered the multiple-choice question about the drivers of generic substitution, believed that they are the main driver for generic substitution practice according to their judgements, while half of pharmacists (53.1%) believed that the driver of generic substitution is patient request (n = 156). The request of physician was the lowest driver as indicated by only third of the responders (35%, n = 103).

When assessing the pharmacists' views on future implementation of generic substitution policy in Jordan, all respondents agreed that the quality use of generic medicines among Jordanian patients can be achieved if both physicians and pharmacists worked together (100%, n = 294), and 85.4% (n = 251) of pharmacists agreed that they should be given the generic substitution right. About two-thirds (69.8%) of the respondents agreed that pharmacists should always dispense the originator prescribed, with 48.3% (n = 142) of the responders agreeing that the substitution process should be allowed only at the request of patients. The pharmacists predominantly agreed that the international non-proprietary name INN prescribing system should be implemented in Jordan (90.1%, n = 265). Most of the respondents (87%, n = 256) agreed that the prescriber should write prescriptions using INN, with the pharmacist dispensing any medicine against the prescription (Table 3).

The pharmacists were asked about profit margin mark-up, 68.7% (n = 202) of them believed that the current profit margin should be increased, whereas 28.6% (n = 84) agreed that it should remain as it is. Only eight pharmacists (2.7%) believed that the current profit margin should be lowered (n = 8).When asked about the profit margin if generic substitution was allowed, 59.2% (n = 174) of them believed that the profit margin should be increased, while 35.4% (n = 104) agreed that it should remain as it is. Only 5.4% (n = 16) of the pharmacists believed that the profit margin should be lowered if generic substitution is allowed.

The measures that should be adopted if generic substitution was allowed were further evaluated. More than half of the respondents (54.8%, n = 161) believed that the generic of patient choice need to be provided, and 41.2% (n = 121) of responders believed that locally produced generic medicines need to be provided. One-third of pharmacists (33.3%, n = 98) believed that the cheapest medicine needs to be provided. Ninety-five (32.3%) pharmacists supported the existence of a list of originator and generic prices to be used by pharmacists to support their generic substitution decision, with a 25.5% (n = 75) believing that the price list of equivalent originators/generics needs to be provided to patients upon request. Other responses given were the need for INN prescription to be implemented, and the supply should be based on patient income status (5.4%, n = 16).

Some pharmacists provided additional information in relation to the topic in question, 'the current tax on drugs which is 4% should be eliminated'.

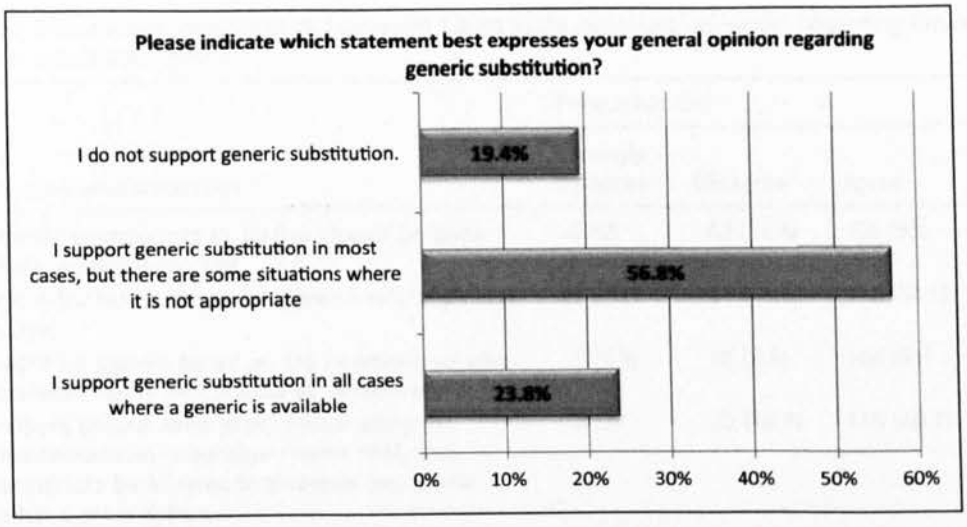

Figure 1. Community pharmacists' general opinion regarding generic substitution.

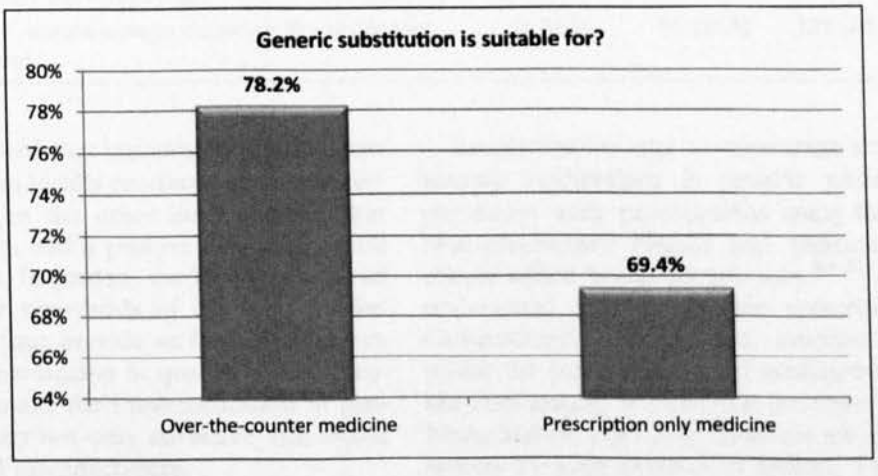

Figure 2. Type of medicines suitable for generic substitution.

Another stated that 'there is no confidence in pharmacists by the patient as many doctors tell them not to accept any change in the prescription therefore the role of the pharmacists should be enhanced and the pharmacist should appear as highly trusted health care provider'. The same pharmacist stated that 'the prescribing physician and pharmacist should have continuous training through the Ministry of Health'.

Discussion

The current legislations in Jordan do not allow pharmacists to perform generic substitution for the prescribed branded medicine. However, the generic substitution is increasingly becoming a worldwide practice, which proves to be an effective mean of economical saving to health care expenditure.[25]

In order to implement a sound generic substitution policy in Jordan, all stakeholders should be involved. The findings from this study revealed that Jordanian pharmacists have positive views on generic medicines in general, in terms of quality, efficacy and safety, with 87.7% of the responding pharmacists believing that generic medicines are bio-equivalents to originator medicines. This confidence in generic medicines was reflected in the supporting of generic substitution in most cases by more than 80% of the responding pharmacists. Similar findings were reported by Allenet et al.[26] in France. They indicated that 90% of the French pharmacists were in favour of the implementation of generic substitution right.[26] Another study in Malaysia showed that more than 90% of community pharmacists believed that they should be granted rights of substitution.[23] However, the

Table 3. Community pharmacists' responses to four-point Likert scale questions on issues regarding future implementation of generic substitution policy.

Question	Survey questions/statement	Frequency (%)			
		Strongly disagree	Disagree	Agree	Strongly agree
1	Community pharmacists in Jordan should be given generic substitution right.	0 (0)	43 (14.6)	150 (51)	101 (34.4)
2	Generic substitution should be allowed only at patient request.	21 (7.1)	131 (44.6)	112 (38.1)	30 (10.2)
3	A prescribing system based on the international non-proprietary name INN should be implemented.	9 (3.1)	20 (6.8)	150 (51)	115 (39.1)
4	Prescribers should write prescription using the international non-proprietary name INN, and pharmacists be allowed to dispense any brand against a prescription.	6 (2)	32 (10.9)	118 (40.1)	138 (46.9)
5	Pharmacy profit margin should be variable according to your professional decision.	13 (4.4)	82 (27.9)	157 (53.4)	42 (14.3)
6	Quality use of generic medicines among Jordanian consumers can be achieved if both physicians and pharmacist work together.	0 (0)	0 (0)	169 (57.5)	125 (42.5)
7	Pharmacist should always dispense the originator prescribed.	14 (4.8)	75 (25.5)	181 (61.6)	24 (8.2)

Malaysian study showed that community pharmacists had little confidence in locally produced generic medicines.[27] This study on the other hand showed that Jordanian pharmacists had a positive view on generic medicines in general. In Jordan, the locally produced generics account for two-thirds of the total market share.[28] The results thus provide an indirect evidence of the trust of the pharmacists in quality of local generics, which would make the implementation of generic substitution policy not only attractive, but would also reward the local manufacturers.

In addition, 204 pharmacists (69.4%) perceived that generic substitution is suitable for POM, which is a similar trend that was reported in the United States (69.2%).[29] However, although most of the Jordanian pharmacists supported generic substitution in most cases, they revealed that there are some situations where the prescribers need to be consulted. The two types of medicines for which the pharmacists preferred to consult the prescribing physician were those with a narrow therapeutic index or controlled drugs. This might indicate the pharmacists' lack of confidence in substituting these medicines. In order to boost confidence, a formulary including information about bioequivalence profile as well as safety of medicines should be developed. This will guide the pharmacists when performing generic substitution. Moreover, the availability of a clear pricing list of bioequivalent generics displayed in each pharmacy can also support pharmacists' decision making.

An alternative way to encourage the utilisation of generic medications is generic prescribing, where physicians write prescriptions using the International Non-proprietary Name, and pharmacists have the choice which brand to dispense.[30–32] In Jordan, it is understood that the generic prescribing is used in Governmental clinics and hospitals. Additionally, under the private insurance arrangements, physicians are encouraged to prescribe the lower priced brands. Nevertheless, currently, there are no mandatory legislations for such practice in Jordan. Therefore, implementing compulsory generic prescribing policy in Jordan would not only draw the attention to the fact that there are alternative available, but patients would also be in a better position to choose between brands. This would have a positive economical impact to the Government as well as patients when lower priced medicines are dispensed. This becomes clearer if we take into account the low annual income per capita of 4350 US dollars in Jordan as per 2010.[33]

In this survey, a significant percentage (90.1%) of the pharmacists was in favour of implementing a compulsory generic prescribing policy system based on the international non-proprietary name INN, with 256 pharmacists (87 %) agreeing with dispensing any medicine against the prescription. Introducing generic prescribing policy is likely to provide additional savings to the health system and consumers. Nonetheless, this can not be applicable as the local industry produces branded generics. Therefore, mandatory generic

prescribing might be expected to have a negative effect on the local generics industry; instead, a brand substitution policy should be implemented. Such policy should clearly state that bio-equivalence is identified between the brands (i.e. branded originator and/or branded generics) and should allow for patient choices to be taken into consideration. Patients' awareness and prescribers and pharmacists training will need to take place for such a policy to be successfully implemented.

Conclusion

The Jordanian community pharmacists have a good knowledge and perception towards generic medicines. Moreover, they hold a positive view regarding locally produced generics. As a result, most community pharmacists in Jordan were in favour of implementing a generic substitution policy. However, such a policy can only be implemented, provided that the bio-equivalence has been established between brands and that the regulators, prescribers and patients agree to it. A formulary of interchangeable medicines and their prices must be developed to guide pharmacists' decision making when performing generic substitution. The Jordanian pharmacists were generally supportive of introducing a compulsory generic prescribing legislation. However, it is inevitable that such policy may be damaging to the local industry, as the majority (97%) of the locally produced generics are branded generics.[28] Therefore, implementing a brand substitution policy is best suited at this stage. However, the pharmacy profit margin will have to be reconsidered if such a policy is implemented.

Study limitation

One limitation of this study is that the views are limited as the majority of the responding pharmacists were employees, while only 25.5% were self or part owner. Since the country operates fixed profit margin to all medicines, generic substitution policy might have a negative impact on pharmacies' profit (i.e. selling originator medicine, which is expensive by nature will make more profits compared to selling the alternative cheaper generics).

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El-Dahiyat and Kayyali *Journal of Pharmaceutical Policy and Practice* 2013, **6**:3
http://www.joppp.org/content/6/1/3

JOURNAL OF PHARMACEUTICAL POLICY AND PRACTICE

RESEARCH Open Access

Evaluating patients' perceptions regarding generic medicines in Jordan

Faris El-Dahiyat* and Reem Kayyali

Abstract

Objective: The aim of this study was to explore Jordanian patients' perceptions toward generic medicines and to evaluate their opinions regarding generic substitution.

Method: A cross-sectional descriptive study involving Jordanian patients was undertaken, using a self-administrated anonymous questionnaire. The response rate was 80% (n=400/500).

Results: The study showed that cost of medicines is high according to 83% of the patients. Most patients (92%) preferred to be prescribed the cheapest medicine. Majority of patients (79%) believed that cost should be considered before a drug is prescribed. Most patients (78%) accepted generic substitution and believed that it can provide significant saving. Surveyed patients (78%) agreed that they should have the option of choosing between generic and originator and 74% believed that physicians should give them that choice. These results showed a significant statistical correlation with the monthly income of the patient, percentage cost they pay and number of medicines prescribed ($P<0.05$).

Conclusion: The high cost of medicines in Jordan is believed to be the main driver for choosing generic medicines Furthermore; patients have positive attitudes towards generic medicines. The involvement of patients in the treatment decision would result in more adherence and improvement in health. The insights gained from patients in this study will be useful to health organisations and policy makers to design a robust generic policy to use medicines cost-effectively in Jordan.

Keywords: Generic medicines, Generic substitution, Cost, Patients, Perception, Policy

Introduction

Generic substitution is the practice of switching from a prescribed originator medicine to an interchangeable generic medicine containing the same active ingredient, dosage form, strength at the time of dispensing [1]. Generic medicines are generally marketed under the non-proprietary name or could be marketed as branded generics [2], as in the case of Jordan where 97% of generic medicines are branded [3].

The generic substitutions practice is increasingly encouraged by health authorities throughout the world [4], and Jordan is no exception. In 2002, a circular from the Jordanian Ministry of Health required doctors in public hospitals and health clinics to prescribe generically. However, if a brand name is prescribed, the patient gets the formulary drug anyway, unless their physician builds a case and receives special permission to have the brand name dispensed. Furthermore, private health insurance companies encourage doctors to prescribe the lowest priced generic [5]. Nevertheless, under the current Jordanian legislation, pharmacists are not permitted to make any change or substitution to prescriptions, unless the pharmacist contacts the prescriber and requests permission for the prescribed originator medicine to be substituted to an alternative generic medicine [6].

The use of cheaper generic medicines is often promoted as a measure to reduce the health care expenditure on pharmaceutical products, and provide savings to patients as well as governments. Generally, the generic medicines are 20-90% less expensive than the innovator medicines [7].

It has been estimated that €25 billion (more than $30 billion) is the annual save made by European patients and health care systems for using generic medicines [7].

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Furthermore, it was reported that the use of generic medicines saved American patients, taxpayers, federal and state governments and other payers $193 billion in 2011 alone, and around $1.07 trillion over the period 2002 to 2011 [8]. A World Health Organisation (WHO) study carried out in several developing countries including Jordan estimated an average saving of 9% to 89% could be made by an individual country from substituting some originator brands to lowest-priced generics [9]. In addition the report stipulated that the saving in Jordan could be 56% if only 11 originator medicines switched to lowest available generics [9].

Despite the financial benefits from using generic medicines, there are still debates regarding generic substitution by patients as well as prescribers, with regards to its effect on patients' clinical outcomes [10-12]. A German study found that half of the primary care patients are sceptical about generic substitution, and 13% of the patients reported that they had experienced new adverse reactions [13]. On the other hand, another study revealed that 61% of the Slovakian patients had positive views regarding generic medicines [14]. The views in the former study were expressed by patients who were more than 60 years of age, chronically ill, and/or without higher education. In the latter study the respondents were predominantly aged 30 years or younger. This indicates that patients' socio demographic characteristics such as educational level, income and age may influence people's opinions of generic drugs [15].

Other factors that may influence patients' attitudes towards generic medicines are believed to be the physicians' prescribing behaviour and their preferences for particular originator brand or their bias against generics [16]. Moreover, the information given by a prescribing physician on generic substitution was also found to be a main driver that influences patients' beliefs about generic medicines and their consumptions [13,17]. Previous studies showed that physicians and pharmacists play an important role when patients choose between branded or generic drugs [18-20]. Therefore efforts to promote generic substitutions practice should be targeted first and foremost at time of prescribing as well as dispensing [21].

Although patient perceptions may play an important role in medication selection, previous research revealed that patients often do not communicate with their physicians about their medicines preference and cost of medications. Furthermore, several studies found that the high out of pocket-costs can be a significant obstacle to medical adherence with prescription medication regimens [22-24]. However, patients can still request generic medications at the point of the clinical encounter or at the time of dispensing of the medication at the pharmacy [25]. In Jordan, over 80% of the cost of medicines purchased by the public is funded through out-of pocket payments [26].

Patient willingness to accept a generic medicine is a core requirement to facilitate the uptake of generic medicines [27,28]. However, there is lack of studies which investigated Jordanian patients' perceptions about generic medicines, their opinions regarding costs of medicines, and their acceptance of generic substitution.

The aim of this study was to assess the understanding and attitude of Jordanian patients' towards generic medicines, their opinions about the cost of medicines in general, and to evaluate their perceptions about generic substitution. The findings from this study would provide a baseline data for establishing a robust generic medicine policy in Jordan.

Methods

This was a cross sectional study where a questionnaire was used to collect data from Jordanian patients whom were targeted by visiting private and public clinics, private and public hospitals, community pharmacies and The National Centre for Diabetes, Endocrinology & Genetics in Jordan. One of the researchers was available on site if the responders need any clarification at the time of the study.

The questionnaire was tested for face and content validity by two experts. It was further revised after pilot testing with 20 patients. Patients were given an information sheet translated to Arabic language by certified translator that explained the research. The questionnaire was also translated to Arabic language by a certified translator.

The questionnaire used consisted of three sections. The first section gave a simple definition of originator and generic medicines with examples. The second section evaluated the preferred prescribed medicines and the perceptions regarding originator to generic substitution and the costs of medicines in Jordan. The last section characterised the respondent demographics.

The responses were framed in four point likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree) questions.

In this study, the sample population was Jordanian patients with chronic medical conditions. From the 500 questionnaires which were distributed, 400 questionnaires were completed and included in this study which gives a response rate of 80%. The participation of patients approached was strictly voluntary and their informed consent was obtained. Anonymity of respondents was preserved in the study, as names of participants were not included.

Data was collected from 15th June 2012 to 26th August 2012. All the collected data were entered into PASW® 18.0 for descriptive analysis using descriptive statistics techniques such as frequency and cross-tabulation and

inferential statistics using chi square tests. This study was approved by the Research Ethics Committee of Kingston University, London.

Results

Demographic characteristics of responding patients

A total of 400 responses were received, with a response rate of 80%, the basic demographic of the responding patients is summarised in Table 1. The sample was almost equally distributed between male (142, 48.3%) and female (152, 51.7%). The majority of the respondents' monthly income was less than 500 JD (59.25%) and holding bachelor degree (42.5%). The respondents mostly pay full cost of their prescription (63.25%) and have more than 6 medicines in their prescription (78.5%) (Table 1).

Table 1 Demographics and characteristics of the responders

Characteristic	*N (%)*
The monthly income	
Less than 500 JD	237 (59.25)
501-1000 JD	84 (21.00)
More than 1001 JD	79 (19.75)
Educational level	
Post graduate	79 (19.75)
Bachelor degree	170 (42.50)
College	62 (15.50)
High school	89 (22.25)
Percentage paid from the prescription cost	
Do not pay at all	81 (20.25)
Pay only a percentage	66 (16.50)
Pay full cost	253 (63.25)
No. of medicines in the prescription	
1-3	29 (7.25)
4-6	57 (14.25)
More than 6	314 (78.50)
Chronic Medical condition	
Cardio-vascular diseases	122 (30.50)
Endocrine diseases	138 (34.50)
Respiratory diseases	95 (23.75)
Other chronic diseases	45 (11.25)
General health Status	
Poor	18 (4.50)
Fair	64 (16.00)
Good	142 (35.50)
Very good	121 (30.25)
Excellent	55 (13.75)

Patients' views on preferred physicians' communications

When assessing the patients' views on preferred communication with physicians, they predominantly agreed that the physician should ask them about their medicines preference (74%, n = 296) (Table 2). There was a significant correlation ($P < 0.05$) between patients' education level and whether or not they prefer to be asked about their medicines preferences (Table 3). As the education level of the responders increased their preferences to be consulted about their medicine choices increased.

Most of the respondents (78%, n = 312) agreed that they should have the option of choosing between generic and originator (Table 2). A chi-square statistic found a significant correlation ($P < 0.05$) between the educational level of the responders and whether or not they should be given the choice between generic or originator (Table 3). Patients with higher education levels tended to agree or strongly agree with being given the choice.

Perceptions on generic substitution

When patients were asked if they mind the pharmacist substituting their prescribed medicine, 75% responders did not mind the substitution to a cheaper equivalent (n = 300) (Table 2). In addition, most patients (78%, n = 312) did not mind their prescribed originator medicine being substituted to a generic one (Table 2). There was a significant correlation ($P < 0.05$) between the patients' monthly income level, percentage cost paid for the prescription and number of medicines in the prescription and whether or not they minded their prescribed medicine to be substituted to a cheaper medicine or a generic. Patients with lower income, pay more percentage of their medicines cost, and are on a higher number of medicines tended to accept the substitution more. The values of chi square are shown in Table 3.

Most responders (63.5%) preferred to accept generic substitution only upon their request (n = 254) (Table 2). There was a significant correlation ($P < 0.05$) between patients' income level and number of medicines in the prescription with their preference for generic substitution to be based on their request (Table 3). Patients with high income levels, and who have small numbers of medicines in their prescription, tended to agree or strongly agree with the substitution being upon their request only. However, there was no correlation with percentage paid from medicines cost and the acceptance of generic substitution upon patients' request. Interestingly, there was no correlation between the education level of the responders and their preference to be consulted prior to originator generic substitution.

Opinions regarding locally produced generic medicines

When assessing the patients' views on locally produced generic medicines, 75% of them preferred to be prescribed

Table 2 Patients' responses to four point likert scale questions exploring their perception about generic medicines

Question	Survey questions/Statement	Frequency (%)			
		Strongly disagree	Disagree	Agree	Strongly agree
1	Physicians should ask patients about their medicines preference.	29 (7.25)	75 (18.75)	174 (43.5)	122 (30.5)
2	Patients should have the option of choosing between generic and originator.	33 (8.25)	55 (13.75)	221 (55.25)	91 (22.75)
3	I don't mind the pharmacist substituting the medicine I was prescribed to a cheaper equivalent one.	8 (2.00)	92 (23.00)	235(58.75)	65 (16.25)
4	I don't mind my prescribed medicines to be substituted from originator to generic. (e.g. Panadol to Revanin).	6 (1.50)	82 (20.50)	228 (57.00)	84 (21.00)
5	My medicines should only be substituted from originator to generic if I request. (e.g. Panadol to Revanin).	69 (17.25)	77 (19.25)	141 (35.25)	113 (28.25)
6	I don't mind the pharmacist substituting my prescribed medicine to an equivalent locally produced one.	3 (0.75)	84 (21.00)	204 (51.00)	109 (27.25)
7	I prefer to be prescribed locally produced medicines.	3 (0.75)	97 (24.25)	178 (44.50)	122 (30.50)
8	I prefer to be prescribed a well-known brand.	158 (39.50)	131 (32.75)	99 (24.75)	12 (3.00)
9	I prefer to be prescribed imported rather than local medicines.	150 (37.50)	143 (35.75)	87 (21.75)	20 (5.00)
10	Costs should be considered before a drug is prescribed.	3 (0.75)	81 (20.25)	220 (55.00)	96 (24.00)
11	I don't mind whether my prescribed / dispensed medicine is locally produced or imported as long as it is effective.	0 (0.00)	85 (21.25)	217 (54.25)	98 (24.50)
12	I prefer to be prescribed / dispensed the cheapest medicine available for the treatment of my condition.	18 (4.5)	14 (3.50)	251(62.75)	117 (29.25)
13	Cost is not an issue for me as long as the medicine will treat my condition.	103 (25.75)	214 (53.50)	41 (10.25)	42 (10.50)
14	A more expensive medicine is a better one.	157 (39.25)	99 (24.75)	69 (17.25)	75 (18.75)
15	Imported medicines are better.	154 (38.50)	127 (31.75)	66 (16.50)	53 (13.25)
16	Using generic medicines would provide significant saving to me.	0 (0.00)	87 (21.75)	229 (57.25)	84 (21.00)
17	In general, medicine costs in Jordan are too high.	3 (0.75)	65 (16.25)	203 (50.75)	129 (32.25)

locally produced medicines (n = 300) and 73.25% patients did not prefer to be prescribed imported rather than local medicines (n = 293) There was a significant correlation ($P < 0.05$.) between patients' monthly income level, percentage cost paid for their medicines and number of medicines in the prescription and their preference for local medicines. Patients with low income, or more percentage cost of medicines and have higher number of prescribed medicines tended to agree or strongly agree with being prescribed locally produced medicines (Table 3). Whereas there was no correlation with the education level of responders and their preference for imported products or locally produced products.

When asked if imported medicines are better than locally produced ones, 70.25% of the surveyed patients disagreed (n = 281) (Table 2). Patients with higher education level, lower income level, pay more percentage cost of medicines and have higher numbers of medicines tended to disagree with imported medicines being better than locally produced ($P < 0.05$) (Table 3).

The majority of patients (72.25%, n = 289) did not prefer to be prescribed a well-known medicine brand with 78.25% agreeing for their medicines to be substituted to a locally produced generic one (n = 313).

In general, the effectiveness of the medicines is the determinant in patients preference not the manufacturer country according to 78.75% of the responders (n = 315) (Table 2).

Jordanian patients' opinions regarding cost of the medicines

The majority of the surveyed Jordanian patients (79%, n = 316) agreed that the costs should be considered before a drug is prescribed (Table 2). There was a significant relationship ($P < 0.05$) between the monthly income of the patient and percentage paid from the cost of medicine and number of medicines in the prescriptions and their agreement. Patients with low income level, who pay more percentage cost of medicines or who have high number of prescribed medicines tended to agree more that costs should be considered before a drug is prescribed.

Patients predominantly (92%, n = 368) preferred to be prescribed and/or dispensed the cheapest medicine available (Table 2). People with low income, high number of medicines in their prescription tended to prefer to be prescribed and/or dispensed the cheapest medicine available for the treatment of their medical condition ($P < 0.05$) (Table 3). However, there was no significant correlation

Table 3 Statistically significant correlations calculated using Chi square test between the statements on the left with each of the demography category investigated

	Survey questions/Statement	Demography criteria			
		The monthly income	*Educational level*	*Percentage paid from the cost*	*No. of medicines in the prescription*
		Chi square value			
1	Physicians should ask patients about their medicines preference.	NS	158.38**	NS	NS
2	Patients should have the option of choosing between generic and originator.	NS	163.53**	NS	NS
3	I don't mind the pharmacist substituting the medicine I was prescribed to a cheaper equivalent one.	52.15**	NS	24.00**	42.03**
4	I don't mind my prescribed medicines to be substituted from originator to generic. (e.g. Panadol to Revanin).	65.12**	NS	45.95**	48.84**
5	My medicines should only be substituted from originator to generic if I request. (e.g. Panadol to Revanin).	146.12**	NS	NS	46.63**
6	I don't mind the pharmacist substituting my prescribed medicine to an equivalent locally produced one.	NS	NS	NS	NS
7	I prefer to be prescribed locally produced medicines.	66.23**	NS	36.02**	55.220**
8	I prefer to be prescribed a well-known brand.	NS	NS	NS	NS
9	I prefer to be prescribed imported rather than local medicines.	16.73*	NS	16.83*	24.69**
10	Costs should be considered before a drug is prescribed.	13.83*	NS	24.07**	43.41**
11	I don't mind whether my prescribed / dispensed medicine is locally produced or imported as long as it is effective.	NS	NS	NS	NS
12	I prefer to be prescribed / dispensed the cheapest medicine available for the treatment of my condition.	21.13**	NS	NS	177.45**
13	Cost is not an issue for me as long as the medicine will treat my condition.	22.65**	NS	40.02**	68.48**
14	A more expensive medicine is a better one.	55.06**	NS	NS	142.07**
15	Imported medicines are better.	21.17**	34.72**	29.26**	134.66**
16	Using generic medicines would provide significant saving to me.	13.23*	NS	92.07**	NS
17	In general, medicine costs in Jordan are too high.	28.59**	NS	46.59**	59.87**

*:p < 0.05, **:P <0.01, NS: non statistically significant correlations found.

between the percentage paid from medicines cost and the preference to be prescribed or dispensed the cheapest medicine available.

Most of the patients (79.25, n = 317) disagreed to the statement "cost is not an issue for me as long as the medicine will treat my condition" (Table 2). A Chi-Square test of independence revealed a significant relationship ($P < 0.05$) between this response and the monthly income of the patient, the% they pay from the cost of their medicines and the number of medicines in their prescription. Patients with low income level, or pay full cost of medicines or are on high numbers of medicines tended to disagree more with the above statement (Table 3).

Most of the patients (64%, n = 256) disagreed that a more expensive medicine is a better one. Patients with low income level or who are on a high numbers of medicines tended to disagree that a more expensive medicine is a better one ($P < 0.05$) (Table 3). However, there was no significant correlation with the percentage paid from medicine cost or educational level and the response to the above statement.

Patients predominantly (83%, n = 332) believed that the medicine costs in Jordan are too high (Table 2). There was a relationship between the monthly income of the patient, the percentage paid from the cost of medicines and the number of prescribed medicines and the agreement to this statement ($P < 0.05$) (Table 3). Patients with low income level, or pay more percentage cost of medicines or are on high number of medicines tended to agree more that medicine costs in Jordan are too high.

Saving from using generic medicines

Most of the Jordanian patients (78.25% n = 313) believed that the use of generic medicines would provide significant saving to them (Table 2). Patients with low income levels, or pay more percentage cost of medicines tended to believe that the use of generic medicines would provide significant saving for them ($P < 0.05$) (Table 3). However,

there was no significant correlation with number of medicines in the prescription and the belief of saving by using generic medicines.

Discussion

In this study, the majority of patients (83%) believed that the costs of medicines in Jordan are too high. Moreover, the costs of medicines were found to be a significant issue for about 80% of the surveyed Jordanian patients, which in turn might affect their adherence to treatments [22-24,29]. These results were mostly reported by low income patients, patients who pay for medicines, and patients who have high number of medicines in their repeated prescriptions.

In low income countries, the health services are believed to be of a poor quality [30] and many of the insurance schemes do not provide medicines benefits, or do so with substantial co-payments [31]. Therefore, medicines are still mainly purchased through out-of-pocket payments [32]. Results from a study in 36 developing and middle-income countries showed that patients purchasing medicines in private sectors pay on average 2.6 times more for originator brands compared to their generic equivalent [33]. This is considered as a barrier to medicines access [34]. In Jordan it was reported that over 80% of the cost of medicines purchased by the public is funded through out-of pocket payments 26 This was reflected in the population of this study, where about 80% of the surveyed patients either paid full or part costs of their medicines.

In the current survey, just under than 80% of the respondents agreed that costs should be considered before a drug is prescribed. In addition, Jordanian patients surveyed predominantly (92%) preferred to be prescribed and/or dispensed the cheapest medicine available for the treatment of their medical condition. Furthermore, the results showed the high trust and confidence of Jordanian patients in locally produced generic medicines. More than third of the respondents preferred to be prescribed a cheaper locally produced generic medicine rather than a more expensive imported brand medicine. Overall, almost 80% of the patients believed that the use of generic medicines would provide significant saving to them.

Most patients (78%) accepted their prescribed originator medicine being substituted to a generic one. With 75% and 78% accepting the pharmacist substituting their medicines to a cheaper one or to locally produced generic one respectively. This was almost the same result of a previous study that was held in Australia where 78.5% of the patients accepted generic substitution based on pharmacists' recommendation [35]. Another study in New Jersey, USA reported that 97% of the patients who had been offered substitution had agreed to switch their therapy [19]. This also corresponds to a study in Finland in which 81% of the participants were of the opinion that cheaper generics were effective and 85% did not consider generics substitution as a threat to drug safety [36]. On the other hand, a Slovakian study reported that only 50% indicated a preference for a cheaper product [14].

In America, 66.7% of the patients requested substitution to generic medications from doctors or pharmacists in most or all time [37]. However, 63.5% of responders in Jordan accepted generic substitution only upon their request, those respondents were mainly the patients with high monthly income, and/or have less number of medicines in their repeated prescription and /or have a full medical insurance. This would indicate that these groups of patients are less sensitive to the cost of medications.

This study found that patients, generally, have acceptability to generic substitution, consistent with previous studies in Denmark, Spain and Norway where preference for the use of generics among patients was reported [38,39].

It was reported that patients' communication with physicians has a key role to promote the use of generic medicines, as their preferences are a powerful motivator to the physicians' prescribing behaviour [40-42]. However, patients hardly ever communicate with their physicians about medication choices and out-of-pocket costs of medications [15,43]. Almost third of the patients in this study believed that they should be involved on decisions regarding their medicines preference, and to have the option of choosing between generic and originator. These beliefs were reported mainly by highly educated participants, similar findings were reported in two different studies in Sweden, in the first study higher educated respondents were 8 times more likely to be involved in choosing and deciding the alternative medicines if available [44]. In the second one, 94% of the patients wanted some involvement in medicine decision making, with positive association between education and shared decision making [45]. Moreover, it is believed that patients who are involved in their medicines decision are more likely to adhere to their treatment with concomitant improvement in health [46].

Physicians' prescribing behaviour can also be influenced by pharmaceutical companies through a variety of incentives such as high-end education programs or even some cash payment for prescriptions [47]. These incentives may indirectly affect the patients, by encouraging them to use higher priced originator-branded products instead of equally effective, lower-cost generics [48]. Therefore, it has generally been agreed that patients should be involved in decisions making about their own health and treatment all over the world [49,50]. Therefore, The Professional Medical Body in Jordan should develop good practice standards that require clinicians to involve patients in treatment choices. This could be through well-designed training

courses that improve the communication skills of doctors, nurses and pharmacists with patients.

From this study, it is clearly obvious that Jordanian patients have a positive attitude towards generic medicines, locally produced medicines, generic substitution, and that they prefer to be involved in medicine treatment selection. This would facilitate the introduction of a generic policy in Jordan which encourages the utilisation of generic medicines through generic substitution and generic prescribing. As a result a huge saving could be achieved to both patients and the health care system.

Conclusion

The high cost of medicines in Jordan is believed to be the main driver for choosing generic medicines which would lead to substantial saving as identified by the findings. Furthermore, patients have positive attitudes towards generic medicines in general and locally produced ones in particular. The involvement of patients in the treatment decision making allow them to choose the preferred medicine, this would result in more adherence and improvement in health.

The insights gained from patients in this study will be useful to health organisations and policy makers to design a robust generic policy to use medicines cost-effectively in Jordan.

Received: 6 April 2013 Accepted: 29 April 2013
Published: 13 June 2013

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Cite this article as: El-Dahiyat and Kayyali: **Evaluating patients' perceptions regarding generic medicines in Jordan.** *Journal of Pharmaceutical Policy and Practice* 2013 **6**:3.

Jordan Journal of Pharmaceutical Sciences, Volume 4, No. 1, 2011

A Comparison of Generic and Originator Brand Drug Prices between Jordan and the United Kingdom

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ABSTRACT

When a pharmaceutical patent expires, generic companies may enter the market and start selling copies of the original drug. As generic drugs contain exactly the same active ingredient, they are certified to be perfect substitutes to the originator branded drugs. In competitive markets, entry of generics would trigger fierce price competition, hence decreasing the monopoly enjoyed by the original patent holder.

The study aims at comparing the retail prices of generics and originator brand for five drugs between Jordan and the United Kingdom and to investigate the relation between the number of generics available, retail price of originator & generic (s) and the effect of time in the market on these prices.

Prices of originators and generics and the number of generics available in each market were obtained from the Jordanian Food and Drug Administration, Royal Pharmaceutical Society of Great Britain, British National Formulary and Chemist & Druggist generics list. The prices were converted to British Pounds expressed per one dose unit. All data were tabulated in spreadsheets; prices were compared between the two countries at different preset times.

The generics of all drugs investigated appeared in the Jordanian market before the patent expiry of their originator worldwide due to lack of patency regulations in Jordan at the launch time of drugs under investigation (before 2004). Unlike the UK, the prices of originator drugs in Jordan did not change when the first generic was introduced to the market. The price of generic drugs has dropped dramatically in the UK at the time of the first generic launch approximately by 90% compared to 15% in Jordan. There was no apparent correlation between the numbers of generics available or the number of years of the first generic being in the market and the prices of the drugs investigated in both countries. The current prices of all investigated drugs in Jordan are higher than the UK particularly for the generics.

Although the income is much lower per capita in Jordan, generic drugs are more expensive than the equivalent prices of the same drugs in the UK.

Keywords: Jordan, United Kingdom, Drug Prices, Originator, Generic.

INTRODUCTION

Drug discovery is a long, difficult, expensive and high-risk process. It begins with basic research, which expands the fundamental understanding of disease pathways, identifies and characterizes new drug candidates. When a pharmaceutical company identifies a New Chemical Entity (NCE), patent protection needs to be acquired. According to the United Kingdom (UK) Intellectual Property Office[1] patent is "An intellectual property right, granted by a country's government as a territorial right for a limited period. Patent rights make it illegal for anyone except the owner or someone with the owner's permission to make, use, import or sell the invention in the country where the patent was granted. As long as renewal fees are paid every year, a UK patent has a life of 20 years and provides protection throughout the UK, but no further". After the patent expiry of the

Received on 10/4/2010 and Accepted for Publication on 21/6/2010.

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originator brand, a generic drug of the same active constituent that is bioequivalent to the originator is allowed to enter the market[2]. Simply, generic product is a copy of an original product whose patent has expired. A patent protects branded drugs from generic competition.

Many studies have explained the effect of patents and other legislation on the returns to innovation, Research and Development (R&D) and market outcomes[3-6]. In general, companies' strategic decisions regarding pricing and investment aim to maximize the profit. Patents are vital for manufacturing in view of the fact that they give the innovator a period during which copying can be excluded and the investment in R&D can be recovered. The manufacturing expenditure of a pharmaceutical is only a small part of the selling price, therefore, an imitator who has no R&D costs to recover can sell a product at a cheaper price and still make a profit[7]. Generics promote innovation as they remove the permanent monopoly on pharmaceutical products. The latter would encourage the originator companies to discover new medicines, and both originator and generic companies to develop new generic equivalents, new formulations, new dosage regimes and new methods of delivery.

After patent expiry, originator drug manufacturers do not necessarily compete on price at the time when generic competitors enter the market, in spite of generic prices being lower than the originator price, the originator price may increase rather than decrease after patent expiry[5, 8, 9]. Even if generics are price competitive, consumers may have loyalty to the originator brand or to another in-patent product[9].

The continuous demand for originator branded drugs while a cheaper generic drug is available means that physicians and patients develop choice habits that are not easily changed[10]. Although residual loyalty remains to the brand after patent expiry, it does not completely deter generic competition[11-12]. This gives a rise to the term 'generics paradox' which predicts that a higher penetration by generics would not necessarily lead to a reduction in originator drug prices[13]; however, it may only prevent a price increase of originator[3]. Patent expiration need not to be the end of the product but with smart marketing it can be a beginning[14].

While it has been concluded that countries with strict price regulation (e.g. France, Italy, Spain) have lower prices for generic drugs compared with countries with less strict regulation (e.g. Germany, Sweden, UK), using cross country data suggested that regulations weaken competition in off-patent markets and that the potential cost-saving out of post-patent competition is not fully realized in countries with tough price regulations[15-18].

Patent expiry does not at all times lead to the entry of generics, and when it does, there is usually a lag time for a few years. After generic entry, the originator pharmaceutical company will not lose all the sales immediately, but only over a period of time. Thus, the value of a patent extends beyond the actual period of patent protection. In addition, the speed with which the original brand loses revenue would appear to be directly proportional to both the size of the market and the price of the original brand prior to generic entry[19].

Entry of generic pharmaceutical products into the market was described as simultaneous rather than sequential[12]. Generic entries are slower on average in markets where there are more brand-name products competing. Furthermore, generic drug entry is faster on average in larger markets, and that entry is faster for drugs that mainly treat chronic diseases[20].

In Jordan, pharmacists are not permitted legally to make any change or substitution to prescriptions, although in practice this happens frequently. If the pharmacist call the doctor and requests the change, then the alternative drug can be dispensed.

The Jordan Food and Drug Administration (JFDA) is in charge for setting the prices of medicines for sale in community pharmacies and private hospitals, but it is not involved in the pricing of medicines obtained through tenders for the public sector. The price of a NCE (originator brand) is allocated based on lowest price resulted out of the following[22]: Cost, Insurance and Freight (CIF) basis, the selling price to the public in the country of origin, the median price in at least 3 countries out of (Britain, France, Spain, Italy, Germany, Greece and the Netherlands), the export price to the Saudi Arabia; a

neighbor country with better negotiating power. The same was applied for generic equivalents provided that it should not exceed 80% of the registered price of the originator (exchange rates were considered and reviewed periodically). Prices were revised after two years of registration and the price of all products are reviewed upon renewal of registration every five years. Where there is a price reduction in the originator drug, all generics must reduce their price, except where the price is due to an exchange rate movement or at the request of the originator.

In the UK, the price of a new pharmaceutical product is indirectly regulated by the Pharmaceutical Price Regulation Scheme (PPRS); a voluntary scheme between companies supplying branded licensed National Health Services (NHS) medicines and the Department of Health (DH)[23]. Through this scheme, the pharmaceutical companies conclude an agreement enabling them to gain a specific return on capital which is set equal to profits from sales to the NHS minus allowable costs. Companies are liberated to set launch prices of new medicines only if they do not exceed the target rate of return on capital. This scheme does not apply to generic medicines and companies are free to set prices of generic medicines. In response to this, the British government introduced a statutory price ceiling for the main generic medicines in 2000[23]. Companies that choose not to become members of the PPRS are subject to statutory price control under section 34 of the Health Act 1999[24].

A comparison between Jordan and UK regarding health and health related issues is illustrated in Table (1).

Table 1: A comparison between the UK and Jordan[21]

Comparison Criteria	UK	Jordan
Population (2006)	60,512,000	5,729,000
Population annual growth rate (%) (2006)	0.4	3.3
Area (sq km)	244,820	92,300
Life expectancy (years) for both sexes (2006)	79	71
Healthy life expectancy at birth both sexes (2003)	71	61
Gross national income per capita (PPP international $) (2006)	33650	4820
Population living below the poverty line (% living on or less than US$1 per day) (2003)	0	<2.0
General government expenditure on health as percentage of total government expenditure (2005)	16	9.5
General government expenditure on health as percentage of total expenditure on health (2005)	87.1	45.3
Private expenditure on health as percentage of total expenditure on health (2005)	12.9	54.7
Private prepaid plans as percentage of private expenditure on health (2005)	7.9	7.4
Social security expenditure on health as percentage of general government expenditure on health (2005)	0	0.7
Per capita total expenditure on health (PPP int. $) (2005)	2598	649
Per capita government expenditure on health (PPP int. $) (2005)	2262	294
External resources for health as percentage of total expenditure on health (2005)	0	4.5

Aims and Objectives

The study aimed to compare the retail prices of generics and originator brands of five drugs from three different classes (omeprazole, lansoprazole, simvastatin, enalapril and lisinopril) in Jordan and UK; particularly:

- compare originator prices at the time of launch and at the time of the first appearance of generic in the market.
- compare current prices of originator brands and generics and their prices at the time of the first generic launch.
- investigate whether there is a correlation between number of generics available and the price change of both originator brand and its equivalent generic.
- investigate whether there is a correlation between number of years originators and generics have been in the market and their prices' change in Jordan and the UK.

Methodology

Data was collected for the five drugs for a maximum period of 23 years (including drug name, strength, price of originator at the time of registration, prices of originator and generics at the time of generic launch, number of generics currently available and current prices for both originator and generics) and obtained from the Royal Pharmaceutical Society of Great Britain, British National Formulary (BNF), updated Chemist and Druggist generic list, JFDA and AstraZeneca-Jordan was also contacted in order to get the price of originator omeprazole at the time of launch.

Two tables were created as excel spreadsheets, one for the UK data and the other for the Jordanian data. In order to avoid package variation in the two countries-if any, prices were set to be as per unit dose using a unified currency for comparison; the Sterling Pound (£) referring to the monthly average exchange rate published by the Central Bank of Jordan[25].

Results: (Prices were in £ per unit dose were mentioned throughout the manuscript).

Generic products of drugs investigated appeared much earlier in Jordan than in the UK e.g. first generic of omeprazole appeared in Jordan 10 years earlier than its equivalent in the UK (1993 vs. 2003) (Table 2).

Table 2: Dates of launch of originator and first generic in Jordan and UK

Drug name	originator launch date		first generic launch date	
	Jordan	UK	Jordan	UK
Omeprazole	1993	1989	1993	2003
Lansoprazole	1996	1994	1997	2006
Simvastatin	1991	1989	1997	2004
Enalapril	1987	1985	1989	2000
Lisinopril	1991	1988	1994	2003

- **Originator Prices At The Time of Launch and At The Time of the first Appearance of Generic in the Market In Jordan and the UK**

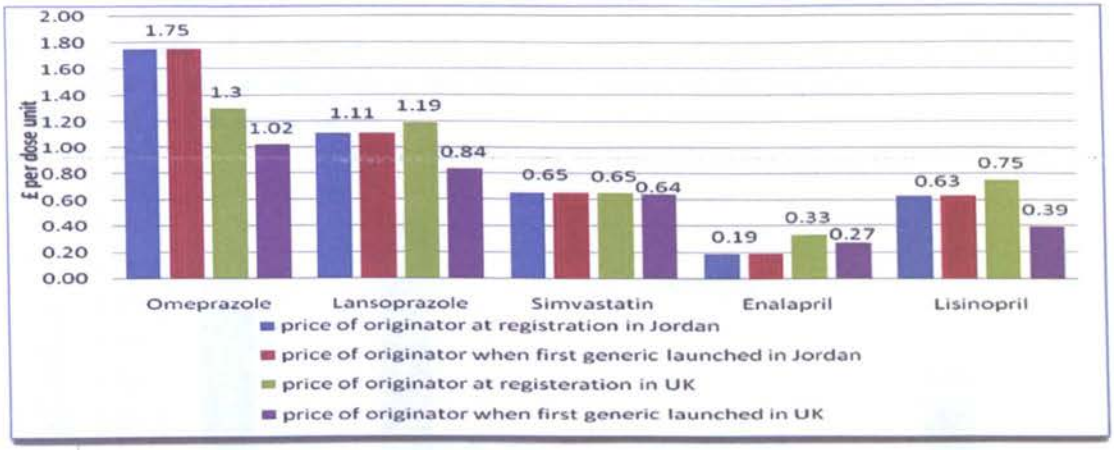

Figure 1: Prices of originators at the time of launch and at the time of the first appearance of generic in the market in Jordan and the UK

As illustrated in Figure 1, the results showed that prices of originators at the time of launch were slightly higher in the UK than in Jordan for lansoprazole, enalapril and lisinopril, with a maximum difference of £0.14 per unit dose for enalapril. The price for simvastatin was the same in both countries, while it was £0.45 higher for omeprazole in Jordan than in the UK. The prices of originator brands in Jordan did not change from the time of the first registration till the time of the first generic launched, however, in the UK the prices of originator drugs fell down when a generic was launched (with the exception of simvastatin in which there was no feasible change). The price of originator brand drugs at the time of launch of the first generic in the market for all investigated drugs except enalapril was higher in Jordan than the corresponding price in the UK. The increase ranged from £0.73 per unit dose for omeprazole to £0.01 per unit dose for simvastatin.The price per unit dose for enalapril in Jordan was £0.08 less than in the UK.

The prices of generic omeprazole, simvastatin and enalapril at the time of the first launch in the UK was higher than the corresponding price in Jordan. This latter increase ranged from £0.11 for enalapril to £0.29 for simvastain per unit dose. On the contrary, the price for lansoprazole and lisinopril in Jordan was higher than in the UK (£0.79 per unit dose for lansoprazole and just £0.08 per unit dose for lisinopril) (Figure 2).

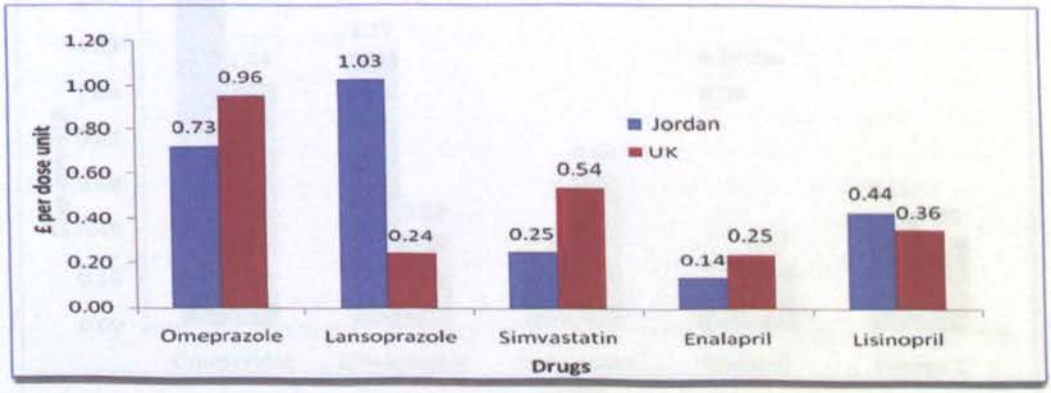

Figure 2: First generic price at the time of the first launch in Jordan compared to the UK

- **Current prices of originator brands and generics and their prices at the time of the first generic launched in Jordan and in the UK**

Generic prices are currently much higher in Jordan than in the UK (Figure 3).

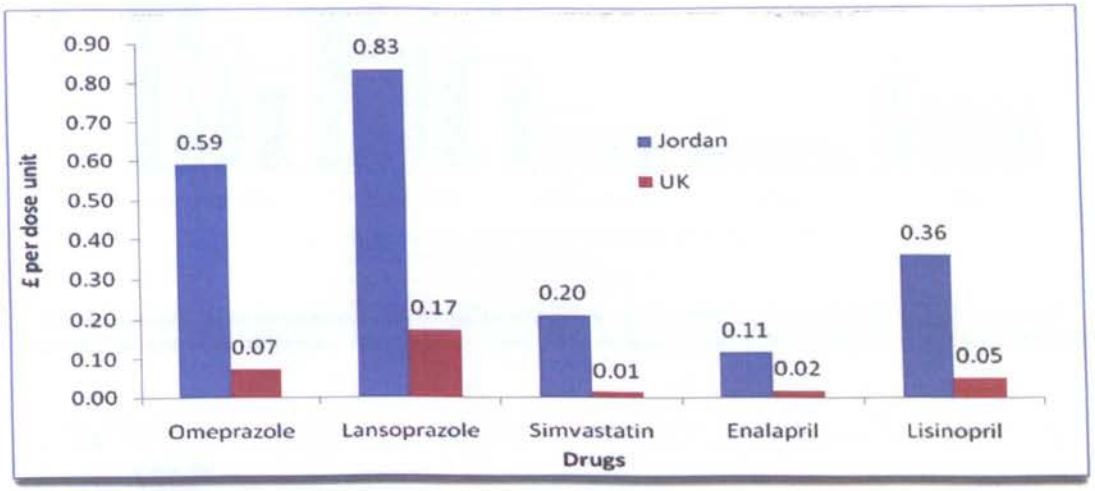

Figure 3: Current prices of generics in Jordan compared to the UK

The current prices of originator brands for omeprazole, lansoprazole and lisinopril in Jordan are higher than their equivalent prices in the UK (Figure 4). However, with the exception of lansoprazole, the current originator prices of the other four drugs under investigation has decreased in Jordan when compared to their equivalent prices at the time of the first generic was launched (Figure 5). For example, the price per unit dose of omeprazole in Jordan was £1.75 at the time of the first generic was launched where it is currently £1.50. While in the UK, the prices of these four drugs were mostly unchanged (Figure 6). On the other hand, unexpectedly there was a big price drop (£0.45 per unit dose) for the originator brand of lansoprazole at the time of the first generic launched in the UK while there was a very slight increase in Jordan for the same brand (£0.06 per unit dose) (Figure 6).

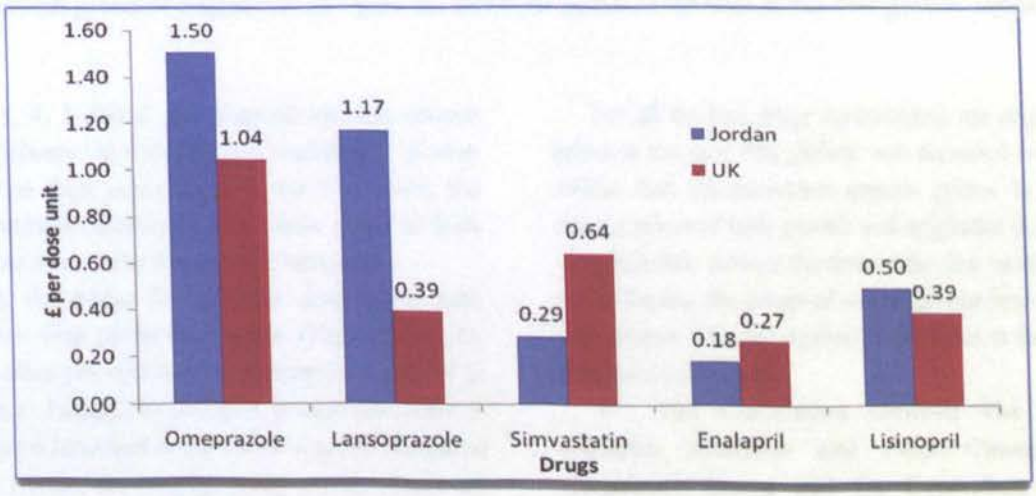

Figure 4: Current prices of originator brand in Jordan compared to the UK

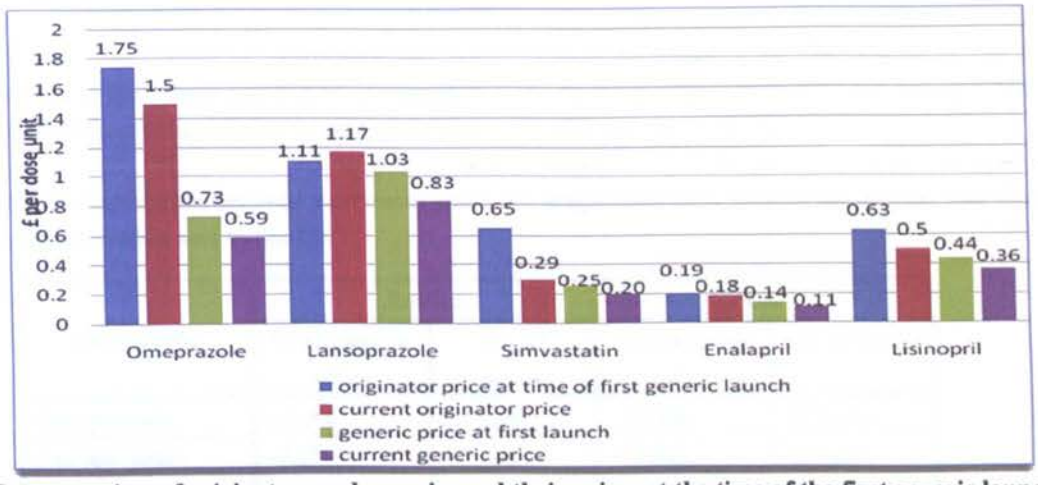

Figure 5: Current prices of originators and generics and their prices at the time of the first generic launched in Jordan

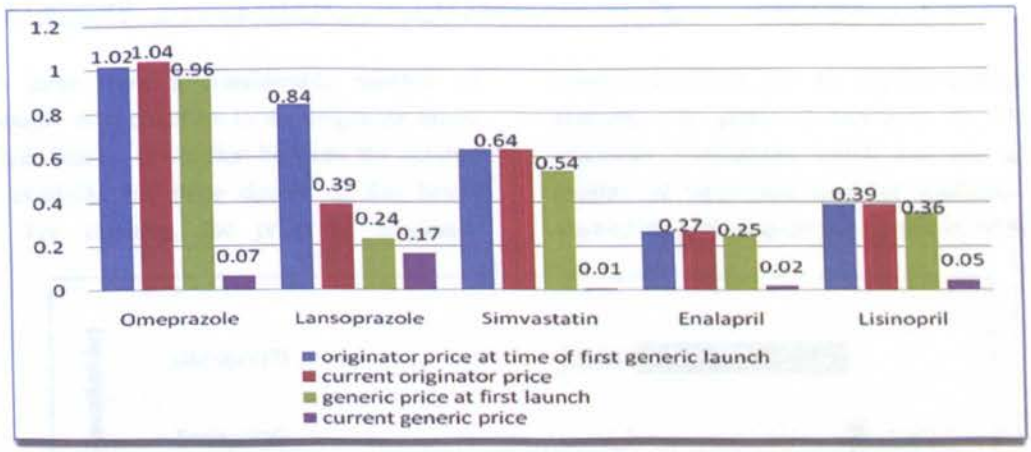

Figure 6: Current prices of originators and generics and their prices at the time of the first generic launched in the UK

Figures 3, 4, 5 and 6 also showed that the current prices of originator simvastatin and enalapril in Jordan are lower than their equivalents in the UK while, the originator enalapril maintained the same price in both countries from time of the first generic launched.

Although the prices for generics dropped in both countries from time of the first launch (Figure 5 and 6), the drop in price per unit dose is substantially greater in the UK than in Jordan. For example, omeprazole price of the first generic launched in the UK was £0.96 compared to £0.73 in Jordan; the corresponding current prices are £0.07 and 0.59, respectively (85% and 19% drop).

For all the five drugs investigated, the originator brand prices at the time first generic was launched were higher in Jordan than the equivalent generic prices. In general, the current prices of both generic and originator drugs in Jordan were less than those at the time of the first launch (Figure 5). As in Jordan, the prices of the originator brands in the UK were higher than the equivalent generics at the time of the first launch (Figure 6).

- **The Correlation between The Number of Generics Available and Price Change of Both Originator Brand and Its Equivalent Generic in Jordan and the UK**

Results showed that prices of originators did not change at the time of the launch/ registration compared to the time of the first generic launched in Jordan while they were decreased in the UK (Figure 1); the percentage of decrease ranged from 67% for lansoprazole to 1.4% for simvastatin (Table 3).

Table 3: Correlation between number of years the originators have been in the market and their prices' change in Jordan and in the UK

Drug name	Jordan		UK	
	% change in price	No. of years	% change in price	No. of years
Omeprazole	+9.0%	15 years	-19.6%	19 years
Lansoprazole	-7.2%	12 years	-67.0%	14 years
Simvastatin	-64.0%	17 years	-1.4%	19 years
Enalapril	+2.5%	21 years	-17.6%	23 years
Lisinopril	-31.4%	17 years	-47.7%	20 years

Although there were a considerable number of generics available as alternatives to the originator brand in Jordan; there was no correlation between the number of generics available and price change of that brand (Figure 7). For example, the price of originator omeprazole which has the highest number of generics available (10 generics) increased by 9%, while the originator simvastatin which has the second lowest number of equivalent generics available (7 generics) showed the highest decrease in price by 64% (Table 3).

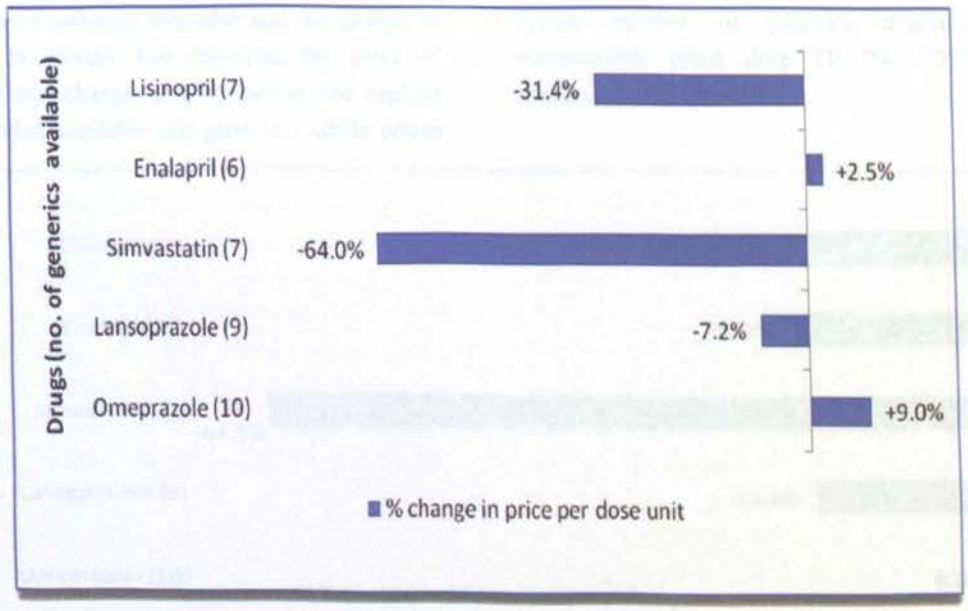

Figure 7: Percentage change in the price of originators from time of the first generic launched in Jordan

The same results were seen in the UK; for example the price of the originator omeprazole which has the highest number of generics available (22 generics) increased by 2.3% while originator lansoprazole which has the lowest number of equivalent generics available (12 generics) showed the highest decrease in price by 53.5% as shown in Figure 8.

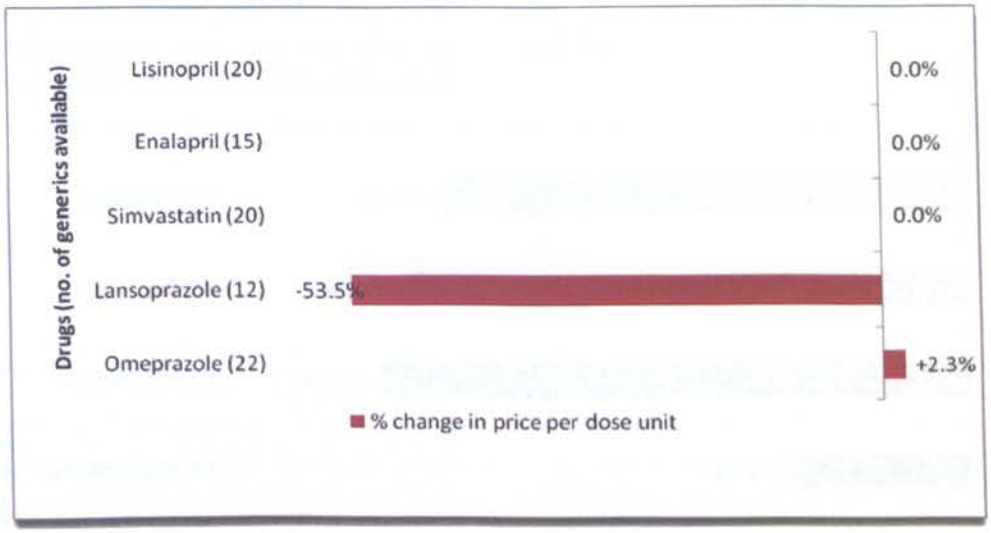

Figure 8: Percentage change in the price of originators from time of the first generic launched in the UK

Again, there seems to be no correlation the between number of generics currently available and the change in generic prices in Jordan. For example, the price of omeprazole did not change despite having the highest number of generics available (10 generics),.while prices of enalapril, lisinopril and simvastatin which have the lowest number of generics available showed a considerable price drop (16.7%, 30% and 64.5%, respectively) (Figure 9).

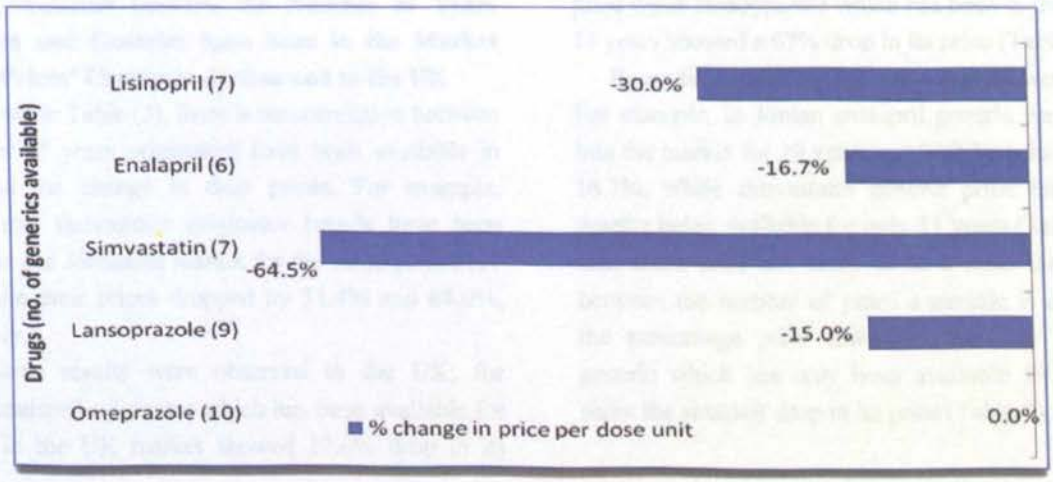

Figure 9: Percentage change in the price of generics from time of the first generic launched in Jordan

Interestingly, for most of the investigated drugs, the drop in the prices of originator brands was much less than the drop in the prices of their equivalent generics in Jordan from time of the first generic launched. For example, originator lansoprazole price drop was 7.2%, when its equivalent generic price drop was 15% and while enalapril originator price increased by 2.5%, there was a 16.7% drop of its equivalent generic price in Jordan (Figures 7 and 9).

On the contrary, with the exception of lansoprazole; while all generics' prices studied decreased much in the UK, the originator prices remained the same (Figure 8 and 10).

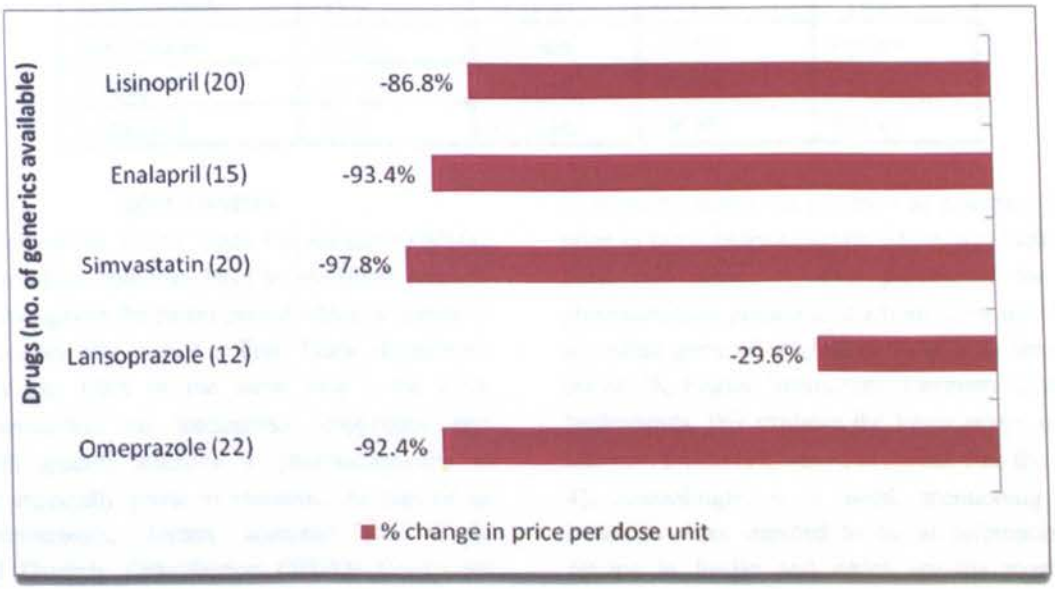

Figure 10: Percentage change in the price of generics from time of the first generic launched in the UK

- **Correlation between the Number of Years Originators and Generics have been in the Market and their Prices' Change in Jordan and in the UK**

As shown in Table (3), there is no correlation between the number of years originators have been available in Jordan and the change in their prices. For example, lisinopril and simvastatin originator brands have been available in the Jordanian market for the same period (17 years) while their prices dropped by 31.4% and 64.0%, respectively.

The same results were observed in the UK; for example enalapril originator which has been available for 23 years in the UK market showed 17.6% drop in its price while lansoprazole which has been in the market for 14 years showed a 67% drop in its price (Table 3).

Regarding generics, the same results were observed. For example, in Jordan enalapril generic was introduced into the market for 19 years in which its price dropped by 16.7%, while simvastatin generic price fell by 64.5% despite being available for only 11 years (Table 4). In the UK, there does not seem to be a clear cut correlation between the number of years a generic is available and the percentage price reduction, however lansoprazole generic which has only been available for 2 years did show the smallest drop in its price (Table 4).

Table 4: Correlation between the number of years generics have been in the market and their prices' change in Jordan and in the UK

Drug	Jordan		UK	
	% change in price	No. of years	% change in price	No. of years
Omeprazole	0.0%	15 years	-92.4%	5 years
Lansoprazole	-15%	11 years	-29.6%	2 years
Simvastatin	-64.5%	11 years	-97.8%	4 years
Enalapril	-16.7%	19 years	-93.4%	8 years
Lisinopril	-30%	14 years	-86.8%	5 years

DISCUSSION

Jordan joined the World Trade Organisation (WTO) in 2000[26] in which countries have to recognise product protection throughout the patent period which is normally 20 years. Jordan also signed a Free Trade Agreement (FTA) with the USA in the same year[27], the FTA provides protection for trademarks, copyrights and patents with specific attention to pharmaceuticals, as patents are especially prone to violation. As part of its trade commitments, Jordan accepted the World Intellectual Property Organization (WIPO) Copyrights and Patents Treaty, this came into effect from April 2004 resulting in new patency regulations in Jordan[28]. Prior to signing the WTO agreement, local companies in Jordan were able to produce generic equivalents of new drugs before patency expiration. The latter explains the availability of generics in Jordan at a much earlier time (Table 2) than in the UK, and may explain why the originator prices did not change after the launch of the first generic in Jordan during that period (Figure 1).

On the contrary, UK has been applying the patency regulations a long time earlier than Jordan. This explains the originator drug prices' being less at the time of the first generic was launched in the UK. This is true for omeprazole, lansoprazole and lisinopril. However, the price of enalapril originator has been found to be less in Jordan and the price of simvastatin originator did not show any change (Figure 1). The latter was explained by that the JFDA is applying pharmaceutical pricing instructions based –in portion- on referring to the drug price in the country of origin which was Netherlands for these two drugs. Another portion of the Jordanian pharmaceutical pricing instructions were stated to refer to a median price of originators in at least three countries out of UK, France, Spain, Italy, Germany, Greece and the Netherlands, this explains the lower prices of enalapril and simvastatin originators in Jordan than the UK (Figure 4). Accordingly, it is worth mentioning that those countries were selected to be as references in drugs' pricing in Jordan and which are the most similar to Jordan in terms of the level of development, income, population, capabilities and health care system.

Although the number of generics available for an individual drug and the number of years since originator or generic was launched, this has been thought to play a big role in dictating drug prices; there was no clear correlation between those factors and price change in Jordan as well as in the UK (Figures 7-10 and Tables 2-3).

Although originator prices in Jordan either decreased or increased after their equivalent generics were introduced into the market (Figure 7), the case is different in the UK in which higher penetration by generics would not necessarily lead to a reduction in originator drug prices[13] (this has been usually called the "generic paradox"); however, it may only prevent a price increase of originator[3] (Figure 8).

Although lower income per capita (Table 1), generics' prices in Jordan are higher than in the UK, this can be

explained by: first; local pharmaceutical manufacturers in Jordan gained an excellent reputation for their good quality products since they have been in the market for more than 45 years that allows them to export for more than 65 countries all over the world including USA and Europe (accounting for 70% of their business), most of which require that exported products should be registered and freely sold in the country of origin (Jordan is the case here) at a price that is considered as a reference price in those export markets, so to encourage export, higher prices at country of origin (Jordan). Second; strict pricing regulations weakens the competition in off-patent time and reduces the potential cost saving from generic drugs[18]; this is the case in Jordan in which current pricing instructions allow what is called branded generic a price ceiling up to 80% of the originator price (Figure 5). Also, lower generic prices in the UK can be explained by the lack of R&D costs for generic manufacturing.

Although lansoprazole generic has been available only for two years, a lansoprazole originator price in the UK was the only one that showed a drop which is considered relatively high (53.5%) (Figure 8), this could be explained by launching FasTab (orodispersible tablet) dosage form besides the capsules.

CONCLUSION AND RECOMMENDATION

Although many limitations were faced in this study; such as lack of published research comparing originator drug prices with generics' drug prices either locally or regionally, limited number of observations (5 drugs investigated), shortage in data (limited number of years) and many differences between the two countries in their level of development, income and health care settings, it can be concluded that a wider extensive study should be conducted in the near future to include more therapeutic classes with different dosage forms for longer time periods with better matching countries that have similar levels of socioeconomic and demographic characteristics of Jordan. Also, it was concluded that the current pharmaceutical pricing instructions in Jordan need to be revised in order to add evidence-based pharmacoeconomic evaluations including cost-effectiveness studies to be required for any new drug entity asks for premium prices, and need to balance the need for lesser generic prices without negatively influencing the local pharmaceutical industry; differential pricing may be an option.

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دراسة مقارنة بين أسعار الأدوية الأصيلة مع نظيراتها الجنيسة ما بين الأردن وبريطانيا

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ملخص

عندما تنتهي فترة حماية الملكية لمستحضر دوائي ما، فإن الشركات المنتجة للمستحضرات الجنيسة تبدأ ببيع نسخة من هذا المستحضر تحتوي على نفس المادة الفعالة تماماً؛ حيث تعد بديلاً مناسباً لتلك المستحضرات الأصيلة وبالتالي تزداد المنافسة ويقل الاحتكار. تهدف هذه الدراسة إلى إجراء مقارنة بين أسعار خمسة أدوية أصيله بمثيلاتها الجنيسة في الأردن وبريطانيا، ومحاولة معرفة إذا ما كان هناك علاقة من حيث الأسعار بين عدد الأدوية الجنيسة المتوافرة ووقت طرحها في السوق.

لقد تم الحصول على المعلومات جميعها الخاصة بهذه الدراسة من المؤسسة العامة للغذاء والدواء في الأردن، ومن الجمعية الملكية البريطانية للصيدلة، بالاعتماد على المرشد العلاجي الوطني البريطاني المحدّث، ومن ثم ترتيبها على شكل جداول لعمل المقارنات المطلوبة. ولقد أظهرت النتائج أن الأدوية الجنيسة كانت قد طرحت في السوق الأردني قبل انتهاء مدة الحماية في وقت الدراسة؛ حيث لم تكن الأردن قد انضمت إلى تطبيق قوانين الحماية العالمية. كما أظهرت النتائج أن أسعار الأدوية الأصيلة في الأردن لم تتغير بعد طرح البدائل الجنيسة على عكس الحال في بريطانيا. كما أن أسعار الأدوية الجنيسة هبط على نحو كبير في بريطانيا مقارنة بالأردن عند طرح هذه الأدوية (بنسبة90% مقارنه مع 15% على التوالي) كما أظهرت الدراسة أنه لا توجد علاقة بين عدد الأدوية الجنيسة المتوافرة وعدد السنوات قبل طرح هذه الأدوية مع أسعارها في كلا البلدين. واستنتجت الدراسة أن أسعار الأدوية التي تمّت دراستها تعد مرتفعة في الأردن بالمقارنة مع بريطانيا. علما بأن مستوى دخل الفرد أقل.

الكلمات الدالة: الأردن، المملكة المتحدة، أسعار الأدوية، دواء أصيل، دواء جنيس.

تاريخ استلام البحث 2010/4/10 وتاريخ قبوله للنشر 2010/6/21.

44.6% (n = 54/121) of nurses, 43.2% (n = 83/192) of community pharmacists, 41.1% (n = 53/129) of hospital pharmacists, 73.7% (n = 14/19) of practice pharmacists and 44.4% (n = 59/133) of patients responding. Overall 70.2% (n = 217/309) of respondents supported reusing medicines, with 89.4% (42) of doctors, 75.9% (41) of nurses, 61.6% (95) of pharmacists and 66.1% (39) of patients stating that reusing medicines would be acceptable. However, only 14.6% (45/309) would reuse medicines unconditionally, with 55.7% (172/309) insisting on some form of check before medicines are reused. For respondents refusing to reuse medicines, the main reasons are show in Table 1.

Table 1: Thematic analysis of why respondents won't reuse medicine

Doctors: Tampering with medicines '. . . *where did it come from*?'; Fraud '*Perverse incentive for pharmacies to re-use returned medication and claim funding twice*'	Pharmacists: Logistics '*how would the NHS Business Service Authority pay us*?'; Quality '*unable to guarantee the quality of the product, even if the packaging is intact and the product looks "fine"* '
Nurses: Tampering with medicines '*Medicines may have been switched*'; Storage '*handled by someone else, not stored correctly, muddled up*'	Patients: Handled by persons unknown '*do not know where they have been*'; Contamination '*catching disease*'

Discussion

This survey of professionals and patients has shown that over two thirds of respondents would support the reuse of medicines returned by patients. Those not supporting the reuse raised important concerns regarding the safe reuse of medicines. Despite the relatively small sample size of this study, there appears to be clear support for medicines reuse. Now is the right time to be undertaking further robust research into the development and testing of processes that would allow for the safe, effective and ethical re-introduction of previously dispensed medicines back into the supply chain.

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0050
Acceptance of generic medicines in Jordan: A study of patients', pharmacists', and physicians' perceptions

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Focal points

- Generic substitution is one way of achieving cost saving for both the public and governments worldwide. However, pharmacists in Jordan are not permitted to substitute any prescriptions.
- This study assessed patients, pharmacists and physicians perceptions towards generic medicines and generic substitution.
- All surveyed stakeholders have positive attitudes towards generic medicines and welcomed the introduction of a policy that encourages generic utilisation such as generic prescribing and generic substitution.
- The findings would provide baseline data to policy makers in Jordan to establish a sound generic policy to enable cost effective use of medicines.

Introduction

Generic substitution is the practice of switching from a prescribed originator brand medicine to an interchangeable generic medicine containing the same active ingredient, dosage form, strength at the time of dispensing [1]. In general, generic medicines are 20% to 90% cheaper than the innovator medicine, and their utilisation represents a well-established strategy for controlling healthcare expenditures [2]. In order to implement a sound generic policy in Jordan, all stakeholders should be involved. Therefore, this study aimed to explore Jordanian patients' and pharmacists' perceptions toward generic medicines, as well as evaluating their opinions regarding generic substitution. Moreover, this study investigated physicians' perception and attitudes toward generic medicines and generic substitution, and it examined factors that affect their pattern of prescribing.

Methods

Three cross sectional self-administrated questionnaire studies involving patients with chronic diseases, pharmacists, and physicians working in both the public and private sectors in Jordan were undertaken. The study was ethically approved by Kingston University ethics committee. The response rate were 80% (n = 400/500), 58.8%, (n = 294/500) and 75.2%, (n = 376/500) for patients, pharmacists and physicians respectively.

Results

Cost of medicines in Jordan was considered high according to 83% of the responding patients. Most patients (92%) preferred to be prescribed the cheapest medicine. Majority of patients (79%) believed that cost should be considered before a drug is prescribed. Cost was also claimed to be an important factor in the prescribing decision for 69.1% of the physicians. 77.4% of the physicians claimed that they often prescribe generic medicines.

Most patients (78%) accepted generic substitution and believed that it can provide significant saving. Surveyed patients (78%) agreed that they should have the option of choosing between generic and originator and 74% believed that physicians should give them that choice. These results

showed a significant statistical correlation with the monthly income of the patient, percentage medicine cost they pay and number of medicines prescribed ($P < 0.05$). However, Physicians mostly (72.1%) opposed to generic substitution being allowed upon patient request.

Most pharmacists had a positive view on generic medicines in general with 87.7% of the respondents believing that a generic medicine is bio-equivalents to the originator. The majority pharmacists (90.1%) were in favour of implementing a compulsory generic prescribing policy. More than 80% of the pharmacists supported generic substitution in most cases. Similarly, physician predominantly (80.1%) welcomed the implementation of prescribing using International Nonproprietary Name (INN) to support generic supply. More than two thirds of the physicians (69.5%) accepted generic substitution by pharmacists. More physicians in the public sector (40.2%) accepted generic substitution compared to the private sector (29.3%) ($P < 0.05$).

Discussion

The findings from this study showed the positive attitude of all stakeholders involved towards generic medications and their high willingness and acceptance of strategies that encourage generic utilisation in Jordan such as generic substitution and INN prescribing. All these strategies would help reduce the high expenditure on drugs in Jordan. These insights will help policy makers in Jordan to develop a robust generic policy which could be used to achieve greater clinical effectiveness and economic efficiency from drug prescribing.

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0051
Enhancing the use of biosimilars in the treatment of chemotherapy-induced anemia (CIA): outcome of an Italian experience

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Focal points

- Biosimilar erythropoietins have lower pricing than originator medicines but they are still under-prescribed by the physicians, expecially in Italy.
- Interchangeability from one branded medicine to a biosimilar must be made only by the physician, such as determined by the Italian Medicines Agency in agreement with other international Position Papers.
- The Department of Pharmacy of the Local Health Unit (LHU) of Palermo, that works for the NHS, promoted various initiatives to increase the use of biosimilars for the ESAs (Erythropoiesis-stimulating agents) naïve patients, in the treatment of CIA.

Introduction

After the patents of branded erythropoietins have expired, biosimilars have been launched in the EU. Such as generic drugs, biosimilars have lower pricing than originator medicines and the clinicians should be consider also economic concerns in their prescriptions. Despite of the presence of clinical EBM regarding efficacy, safety, quality and the cost saving, the use of biosimilars in Italy is still low(16%), especially in Sicily(2%).

The Department of Pharmacy of LHU Palermo enhanced the use of biosimilars in all the County organizing two education courses and publicizing many cost-efficacy evaluations to promote independent assessment on this pharmaceuticals.

The Department focalized the area for intervention only in the ESA naïve oncology patients. In fact, while substitution with generic drugs can be done at the hospital pharmacy or retail pharmacy level, the National Regulations stated that interchangeability from one biopharmaceutical branded medicine to a biosimilar must be made only by the physicians, because these formulations may differ from the original and may cause immunogenicity.

Since January 2013, the Department stated that in each naïve patient receiving an erythropoietin for the chemotherapy-induced anemia the hospital pharmacists dispense the cheapest product containing the prescribed substance. All the physicians were informed about this initiative. The physician can prohibit drug substitution by stating 'do not substitute' in the form and adding a valid justification.

Methods

The Department of Pharmacy centralized the distribution of all the prescriptions containing ESAs in their 14 hospital pharmacies spread on County. These pharmacies collected all the data related to the outpatients receiving ESAs both in an electronic database and in a paper folder. Copy of all the prescription forms related to the naïve oncology patients in Palermo were retrospectively analyzed.

The observed period was the first quarter of 2013 compared with every quarter of 2012.Ethic approval was not required.

Results

In the first quarter of 2013, after our actions, 38 naïve patients, on the total numbers of 90 naïve oncology patients, were treated with biosimilars (42 %). Data from 2012 showed respectively for each quarter 5%, 12,5%, 10% and 15% of the patients receiving biosimilars.

The use of epoetins for CIA was appropriate in all the cases. The treatment was in fact prescribed when the Hb values was in the range (80 g/L–100 g/L), according to the Italian Law. We can also state that no spontaneous reports of suspected adverse

the Department of Bio-Surgery and Surgical Technology, Imperial College, London. Each interview lasted from 45 min to an hour. Topics discussed included medication reconciliation, plan-do-study-act (PDSA) cycles and FMEA. All interviews were thoroughly read first and then recurrent themes related only to the FMEA data were identified and listed. An initial coding frame was then constructed for a sample of four interviews by the researcher and revised by a second researcher. Differences in the coding were discussed and the revised final coding frame was used to develop additional themes from the remaining 18 interviews. Ethics approval was granted by the Leicestershire, Northamptonshire and Rutland Research Ethics Committee.

Results

In total, 22 interviewees participated, but themes were identified from 21 interviewees who have completed the FMEA. One interview was excluded because the interviewee did not participate in the FMEA. The themes identified included the perceptions and experiences of participants with the FMEA, validity and reliability issues and FMEA's use in practice. FMEA was defined by participants as a structured subjective process that helps healthcare professionals get together to identify the high-risk areas within a process of care. Both positive and negative opinions were expressed with the majority of the interviewees expressing constructive views towards FMEA in terms of it being a useful tool particularly for mapping and identifying problems within a process of care. Other participants criticised FMEA for being subjective and lacking validity. The limitations that were most likely to restrict its widespread use were its time-consuming nature as well as the perceived lack of validity and reliability. Participants felt that initial proper training for FMEA was important and that team composition appeared to be an important factor that affected the FMEA results.

Discussion

This is the first time that participants of FMEA in the UK have been interviewed to account their opinions and familiarities with FMEA. This study will help other hospitals, planning to incorporate FMEA, to gain insight about FMEA's benefits and limitations. This would assist the hospitals to explore the means by which they can optimise the success and benefit of FMEA while minimising its shortcomings before investing the resources, time and effort.

Acknowledgement

This research has been funded by the Health Foundation.

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A comparison of generic and originator brand drug prices between the Hashemite Kingdom of Jordan and the United Kingdom

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Background

When a pharmaceutical patent expires, generic companies start selling copies of the original drug containing the same active ingredient. Generics trigger price competition and decrease the monopoly enjoyed by the original patent holder. Generic manufacturers do not have research and development costs and thus sell their products cheaper.[1] This study was aimed to compare retail prices of generics and originators of five drugs (omeprazole, lansoprazole, simvastatin, enalapril and lisinopril) between Jordan and UK to determine the effect of time in the market and number of generics available on the price of both originator and generic.

Method

The study was conducted in summer 2008 and it adopted a methodology by which data-collection-tool spreadsheets were created to record the prices of originators and generics and the numbers of generics available in each market at time of first launch and at the time of the study. Ethics approval was not deemed necessary. The main sources of data were the Jordanian Food and Drug Administration, the British National Formulary and Chemist and Druggist generics list. The prices were converted to British Pound and were expressed per one dose unit.

Results

The generics of drugs investigated appeared in the Jordanian market before patent expiry of their originator worldwide. Prices of originator drugs dropped when first generic of the same drug or the same class of drug was introduced in the UK. Originator drug prices in Jordan did not change when first generic was introduced. For example, the price of omeprazole in Jordan stayed at £1.75/dose unit, whereas in UK it dropped from £1.30 to 1.02/dose unit. The price of generic drugs from time of first launch until August 2008 has dropped by approximately 90% in the UK compared with a drop of only 15% in Jordan. For example, the price of enalapril fell by 93.4% in the UK compared with a drop of only 16.7% in Jordan. There was no apparent correlation between number of generics available or number of years of availability of generics on the market and the prices of the drugs investigated in both countries. The current prices of all investigated drugs in Jordan are higher than UK particularly for the generics. For example, the current price for generic lansoprazole in Jordan is £0.83/dose unit compared with £0.17/dose unit in UK.

Discussion

The patency law regarding pharmaceutical products has only been applied in Jordan since 2004,[2] and this may partly explain the launch date of generics and their corresponding prices in Jordan. In Jordan, generics are prescribed by brand name, unlike the UK where generic names are used, and in both countries, pharmacists are not permitted to make any change or substitution to prescriptions written with brand names for either generics or originators. Generic drugs are relatively expensive in Jordan and are 5–20 times more expensive than the equivalent prices of the same drugs in the UK. This was surprising considering the difference in income per capita between the two countries (seven times lower in Jordan).[3] Recommendations were made to make drug prices more affordable to the public in Jordan.

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Why don't patients with metabolic syndrome achieve recommended blood pressure targets? A pilot study in the United Arab Emirates

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Background

In the United Arab Emirates (UAE), blood pressure (BP) control remains suboptimal in many treated hypertensive patients despite the availability of effective management strategies.[1] There are many contributing factors to poor BP control that range from patients' non-adherence to physicians' lack of hypertensive therapy intensification also known as clinical inertia. The metabolic syndrome, a clustering of metabolic abnormalities such as hypertension, diabetes, dyslipidaemia and obesity enhances the probability of uncontrolled BP.[3] This pilot study examined the relative importance of these influencing factors on BP in a hypertensive population living in the UAE.

Method

In this retrospective pilot study, the medical files of 100 out of 1412 potentially hypertensive patients (aged 28–80 years) with available data for metabolic and cardiovascular evaluation and without history of cardiovascular diseases (CVD) were randomly selected and manually accessed. Physicians' adherence to clinical guidelines in CVD prevention was assessed using a validated medication-assessment tool.[3] The international diabetes federation definition of metabolic syndrome was adopted. BP was considered controlled when three consecutive blood BP readings were ≤140/90 mmHg (or ≤130/80 mmHg if diabetic), or uncontrolled if this target was not achieved. Patients were classified into two groups based on BP readings. BP control was evaluated in relation to metabolic abnormalities, adjusting for age and gender. Ethics approval was obtained from the research committee of Skeikh Khalifa Medical City.

Results

Females represented 71% of the study sample and patients with uncontrolled BP represented 59%. There were no significant differences in other variables between the two controlled and uncontrolled BP groups. HbA_{1c}, fasting blood glucose and number of antihypertensive drugs prescribed were higher in patients with uncontrolled BP ($P < 0.05$). Although physicians' adherence to guidelines in both BP groups was high but not significantly different, achieving target value of total cholesterol in patients prescribed a statin showed low adherence to guidelines in the uncontrolled BP groups (48.9% compared to 71.9% in the controlled BP group). Clinical inertia was observed in 12.5% of patients with uncontrolled BP. Logistic regression suggested that the study hypothesis is accurate; however due to the small sample size this couldn't be considered conclusive.

Discussion

This pilot study highlighted the limited data available in the research setting. Due to the lack of patients' electronic medical database, patients' medical files were manually accessed limiting the number of data sets available during the data-collection period. International coding of diseases was unavailable, therefore indicator drugs were used rendering a lot of potential subjects unidentifiable and slowing down the data-collection process. Despite these limitations, coexisting metabolic abnormalities in hypertensive patients with the metabolic syndrome appeared to influence BP control. Poorly controlled HbA_{1c} and fasting blood glucose were greatly associated with uncontrolled BP, which agrees with previous studies.[3] The pilot also demonstrated that some clinical outcomes could be better explained by exploring patients' and physicians' perception of the holistic management of the metabolic syndrome; therefore, a qualitative approach is currently taking place to help identify some of the key behavioural factors that influence BP control and are specific to patients residing in the UAE.

to new medicines. Our goal was to determine the time period between the registration and reimbursement date in Hungary. METHODS: We selected all newly reimbursed pharmacy drugs between January 2004 and April 2010 and looked for the date of registration and reimbursement in public websites and Bulletins of EMEA/EMA, National Institute of Pharmacy and National Health Insurance Fund. We excluded hospital only medicines and drugs with special reimbursement budget from the analysis due to the lack of transparency of reimbursement dates in publicly available data sources. RESULTS: 106 newly reimbursed innovative medicines between January 2004–April 2010 were included into the analysis. The average time period between registration and reimbursement was 677 days. CONCLUSIONS: Hungary joined the European Union in May 2004 and implemented the EU Transparency Directive. Time to reimbursement of innovative medicines in Hungary is significantly longer than the recommended 90 + 90 days for pricing and reimbursement process set by Transparency Directive. The pricing and reimbursement process in Hungary takes more time than in 15 European countries included in the EFPIA Patients W.A.I.T. indicator database (from 101 to 403 days). Acceleration of patient access to innovative medicines is highly recommended in Hungary.

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THE IMPACT OF THE HOSPITAL FUNDING SYSTEM ON THE RANGE OF THE EXPENSIVE DRUGS AVAILABLE IN FRENCH AND ENGLISH HOSPITALS

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OBJECTIVES: In French and English hospitals, there are a lists of drugs financed out of scope of casemix-based payment system that are Payment by Result (PbR) and "Tarification à l'activité" (T2A). We examined a difference in the range of these drugs in both countries. METHODS: In the study were included the drugs registered on the list "en sus" in French system, the drugs from the high cost drugs list (HCD) and from the oncology regimens list in English system. The information is available in official sources. The number and overlap of entities excluded from the casemix-based payment system in two countries were determined, as well as similarity rate. RESULTS: 210 entities are financed out of scope of casemix-based payment system in England and 101 in France. 69% (145/210) of entities excluded from PbR are not on the list "en sus". Around 36% (36/101) of entities excluded from T2A are not on the English lists. There are 65 entities common for both lists; 51% (33/65) are from ATC class L (antineoplastic and immunomodulating agents). Four ATC classes have none common drugs. The aim of the list in two systems is fair reimbursement of the expensive drugs within the casemix-based payment system. In French system this list is used also to improve the access to the expensive and innovative drugs. So, 50% (73/145) of the entities excluded from PbR and not included on the list "en sus" are on another list in French system, the retrocession list. CONCLUSIONS: There is a difference in the range of drugs financed out of scope of casemix-based payment system in French and English hospitals. More drugs are excluded from the casemix-based payment system in England, but it does not facilitate access to new drugs.

PHP36

THE AVAILABILITY AND FUNDING OF ORPHAN DRUGS IN BOSNIA AND HERZEGOVINA IN COMPARISON WITH NEIGHBORING COUNTRIES

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OBJECTIVES: The aim was to examine the current availability and funding of orphan drugs in both entities of B&H and compare the obtained data with neighboring countries (Croatia, Serbia and Montenegro) and the EU. METHODS: We have analyzed the current published list of medicines in B&H and neighboring countries. We have compared the drugs that have the status of orphans according to the Orphanet report. RESULTS: In BiH there are no lists of orphan drugs while some of them are included in the list of chemotherapeutic agents and drugs for specific diseases (RS). Only Croatia has made a special list of expensive medicines containing drugs for treatment of hereditary enzyme deficiency. All countries have imatinib reimbursed. Only in the RS and Serbia thalidomide is reimbursed, and Serbia has listed sildenafil, zinc acetate and busulfan. Present practice in all countries is that patients apply individualy for orphan drugs reimbursement approval to HIFs. CONCLUSIONS: In order to improve access to orphan drugs it is necessary to adopt a national policy which will be harmonized with the EU. Decisions on the reimbursement must be based on real possibilities and it is necessary to implement appropriate registries for future resource allocation decissions.

PHP37

THE IMPACT OF UNIVERSAL COVERAGE ON EQUITY IN HEALTH CARE FINANCE AND FINANCIAL RISK PROTECTION IN THAILAND

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OBJECTIVES: To assess the impact of achieving universal coverage (UC) on equity in health care finance and on financial risk protection from expensive medical care costs for Thai households. METHODS: Secondary data analyses using nationally representative household surveys conducted by National Statistical Office, the Socio-economic Survey 2000 (prior to UC) and 2002–2006 (after UC) to analyze changes in progressivity of overall health care finance and different health financing sources. The share of households facing catastrophic health expenditure in the poorest and richest income quintiles prior to and after achieving UC was also assessed. RESULTS: The financing of the Thai health care system became more equitable after the UC policy was implemented. Improved financial risk protection after achieving UC was observed due to the comprehensive benefit package and literally free at point of services. The Kakwani index value for overall health care finance changed from –0.0038 (regressive) in 2000 to positive (progressive) values of 0.0014, 0.0342 and 0.0406 in 2002, 2004 and 2006, respectively. The share of households facing catastrophic spending on health decreased from 5.4% in 2000 to 2.0% in 2006. The 1st (poorest) quintile experienced a 77.5% reduction in the proportion of households facing catastrophic health expenditure, while there was a 41% reduction in the share of households in the 5th (richest) quintile. CONCLUSIONS: Factors contributing to equitable health finance are: the increasing share of progressive financing sources in particular direct tax; the decreasing share of the regressive out-of-pocket payments for health. Using general taxation to finance the poor and the informal sector not only helps reach universal coverage, it is also the most progressive financing source. Various factors contribute to the low incidence of catastrophic heath expenditure: comprehensive benefit package covering almost all health services which are free at point of use, and well-functioning primary care providers.

PHP38

HOW EQUITABLE OF HEALTH SERVICE USE AND GOVERNMENT SUBSIDIES IN THAILAND AFTER ACHIEVING UNIVERSAL COVERAGE?

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OBJECTIVES: To assess trends of equity in health service use and distribution of government subsidies to ambulatory services and hospitalization across income gradients of the Thai population prior to and after implementation of the universal coverage (UC) policy in 2002 and explained how such equity has been achieved. METHODS: Secondary data analyses using nationally representative household surveys conducted by National Statistical Office, the Health and Welfare Survey (HWS) 2001 (prior to UC) and 2003–2007 (after UC) to analyze equity in health service use at different health care levels and the distribution of government subsidies for health. The analytical approach employed a standard method for health equity analysis of the large scale household surveys proposed by O'Donnell et al. RESULTS: Outpatient and inpatient service use of the Thai health systems were both pro-poor before achieving UC in 2002 due to various government interventions in extending health insurance coverage and countrywide distribution of health service infrastructure, and the significant increase in human resource production. After the UC policy implementation, the pro-poor service utilization was further progressed. Overall, public subsidies for health were found to be pro-poor for both outpatient and inpatient services with the concentration indexes of –0.226, –0.186 and –0.180, in 2003, 2006 and 2007, respectively. District health provider networks, in particular health centres, district and provincial hospitals are the major determinants of the pro-poor distribution of service utilization and public subsidies, due to their geographical proximity and better access by the poor. A comprehensive benefit package and the provision of services that are free at the point of use resulted in the pro-poor benefit incidence. CONCLUSIONS: The pro-poor outcome is the result of an availability of functional primary care at the district level, and implementation of the UC policy which focuses on contracting primary care networks at the district level.

PHP39

A COMPARISON OF GENERIC AND ORIGINATOR BRAND DRUG PRICES BETWEEN JORDAN AND THE UNITED KINGDOM

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OBJECTIVES: The study aimed to compare the retail prices of generics and originator brand for five drugs between Jordan and United Kingdom and to investigate the relation between number of generics available, retail price of originator and generic (s) and the effect of time in the market on these prices. METHODS: Prices of originators and generics and the number of generics available in each market were obtained from the Jordanian Food and Drug Administration, Royal Pharmaceutical Society of Great Britain, British National Formulary and Chemist & Druggist generics list. The prices were converted to British Pounds expressed per one dose unit. All data was tabulated in spreadsheets; prices were compared between the two countries at different preset times. RESULTS: The generics of all drugs investigated appeared in the Jordanian market before patent expiry of their originator worldwide due to lack of patency regulations in Jordan at the launch time of drugs under investigation (before 2004). Unlike the UK, the prices of originator drugs in Jordan did not change when the first generic was introduced to the market. The price of generic drugs have dropped dramatically in the UK at time of first generic launch approximately by 90% compared to 15% in Jordan. There was no apparent correlation between the numbers of generics available or the number of years of first generic being in the market and the prices of the drugs investigated in both countries. The current prices of all investigated drugs in Jordan are higher than the UK particularly for the generics. CONCLUSIONS: Although much lower income per capita in Jordan, generic drugs are more expensive than the equivalent prices of same drugs in the UK