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**THE AMERICAN UNIVERSITY IN CAIRO**  
**الجامعة الأمريكية بالقاهرة**

**School of Global Affairs and Public Policy**

**THE PHARMACEUTICAL SUPPLY  
OF BRAND AND GENERIC MEDICINES  
FOR DIFFERENT RURAL AND URBAN AREAS IN EGYPT**

**A Thesis Submitted to the**

**Public Policy and Administration Department**

**in partial fulfillment of the requirements for the degree of  
Master of Public Policy**

**By**

**Yasin M. Ragaey Afify**

**Spring16**

**The American University in Cairo  
School of Global Affairs and Public Policy  
Department of Public Policy and Administration**

**THE PHARMACEUTICAL SUPPLY  
OF BRAND AND GENERIC MEDICINES  
FOR DIFFERENT RURAL AND URBAN AREAS IN EGYPT**

**Yasin M. Ragaey Afify**

Supervised by:  
Dr. Hamid Ali

Chair of Department of Public Policy and Administration

**ABSTRACT**

Medicines are an important intervention for protecting public health. While medicines have brand and generic type products, those used for treating non-communicable diseases are used by patients for life.

The pharmaceutical market is not a competitive market with asymmetric flow of information. Equal access to both types of medicines is part of equal access to health care in different socioeconomic areas. Patients with non-communicable diseases should own their choice of whether brand or generic medicines for their treatment not the market supply that dictates their consumption.

In this thesis, we used data for availability of 39 medicines treating non-communicable diseases selected based on some inclusion criteria.

Our hypothesis assumed social equity that presumes equal access to both medicine types in varying rural and urban areas where population having chronic conditions have to acquire their treatments for life. Data was modeled and logistic regression was used. Results were produced using statistical software; both SPSS and R.

Primary findings show that rural and urban areas have different pattern of market supply for both brand and generic medicine types. In the same settings of a socioeconomic area, the probability of supply of brand rather than generic medicines increases by the increase in price.

Social health insurance coupled by pharmaceutical Track and Trace system and combined pricing mechanisms should be in place to insure equilibrium between market supply and equal access to medicines. Patients with non-communicable diseases in different urban and rural areas in Egypt should be left to consume their medicine type at their choice. Guidelines for promotion of prescription medicines, guidelines for prescribing practices should be in place to improve the market equilibrium.

## **Acknowledgement**

First and foremost, I thank Allah for all successes in my life and how my life was and how it will be.

This thesis is a product of not only my efforts and work, but also the support of all people surrounding me without their help I wouldn't be able to achieve any of it.

I am grateful to Dr. Hamid Ali for his support, understanding not only in supervising this thesis but also along the program.

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I am thankful to my parents who are supporting and encouraging me through my whole life, I am grateful for all what they did to me as they are the reasons for what and where I am today. I am grateful to my wife who is always there to my side putting all her possible efforts to our life and her support for taking any step forward.

Finally, my thanks go to Yousef Jameel and his Public Leadership program, which I had been part of, without which this thesis wouldn't have been written and produced.

### **Dedication**

I dedicate this work to all patients; Egyptians and worldwide, who need some light to be shed on their needs, and who need fair treatment policies and adequate social life.

I direct this thesis towards healthcare system stakeholders and policy makers, whether public or private, to utilize this work presented here for the sake of patients.

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## List of Abbreviations

ATC: Anatomical Therapeutic Chemical Classification  
BMI: Business Monitor International  
CAPA: Central Administration of Pharmaceutical Affairs  
COPD: Chronic Obstructive Pulmonary Disease  
CVS: Cardiovascular  
EML: Essential Medicines List  
ERP: External Reference Pricing  
GDP: Gross Domestic Product  
HAI: Health Action International  
INN: International Nonproprietary Name  
IP: Intellectual Property  
LMIC: Low- and Middle-Income Countries  
MA: Marketing Authorization  
MNCs: multinational corporations  
MOH: Ministry of Health, Egypt  
MSF: Médecins sans Frontières  
NCD: Non communicable Disease  
OOP: out-of-pocket  
PE: Pharmaco-economics  
PPRI: Pharmaceutical Pricing and Reimbursement Information  
R&D: Research and Development  
RPS: Reference Price System  
TRIPS: Trade-Related Aspects of Intellectual Property Rights  
WB: World Bank  
WHO: World Health Organization  
WTO: World Trade Organization

## Keywords:

**Pharmaceutical – pricing - Brand – Generic - Urban- Rural- Socioeconomic – Availability- Access to Medicine – Non-communicable diseases (NCD) - social equity**



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## **Introduction**

### **Global Market**

Medicines are important intervention device to preserve and improve people's health. It is a major input for improving health outcomes when it is provided in the right place and in right time. Regardless of the patients' socioeconomic classification, health is always their naturally granted wealth sought to be kept in a well-being status.

The global pharmaceuticals market is worth US\$300 billion a year, a figure expected to rise to US\$400 billion within three years (WHO, 2016). The 10 largest drugs companies control over one-third of the global market, several with sales of more than US\$10 billion a year with a profit margins of about 30 percent.

Medicines account for 20–60 percent of health spending in Low- and Middle-Income Countries (LMIC) compared to 18% in countries of the Organization for Economic Co-operation and Development (OECD). In developing countries, up to 90 percent of the population purchases medicines through out-of-pocket payments, making medicines the largest household expenditure item after food. As a result, medicines, particularly those with higher costs, may be unaffordable for large sections of the global population and are a major burden on government budgets (WHO, 2016).

Increasing expenditures on drugs put pressure on policy makers to control drug costs and ensure that these resources are well spent. Pharmaceuticals make an important contribution to people's health. However, drugs are frequently not used appropriately (OECD, 2002). Rational use of medicines and proper prices will decrease these expenditure and lower that pressure on policy makers.

Expenditure on pharmaceuticals in US was \$235 billion in 2005, while for OECD countries it was \$569 billion (OECD, 2008). The pharmaceutical expenditure share of health care expenditure varies from 19 % in high income countries to 30% in low income countries (WHO, 2011). Whether prices of medicines are determinant of total expenditure on health or not, equal access to medicine is a right for all people. Initiatives to stimulate availability and access through manufacturing innovations,

procurement mechanisms, or supply chain improvements require management of pricing to have sustainable impact.

Pharmaceutical pricing regulations can be found in most of the European and Middle Eastern countries (Wertheimer et al, 1992). Pricing policies set as part of government intervention is necessary to achieve public health objectives and to mitigate any market (Quick, 1997). Some countries, such as France and Italy, regulate drug prices directly through price control; others, such as Australia, Germany, Japan, India, Peru, Bolivia, Guatemala use other measures to directly or indirectly control prices (Danzon, 2000).

### **Egypt Context**

The pharmaceutical market in Egypt is one of the largest in the Middle East and Africa (Al-Ali, 2002). It is worth around \$4.4billion as foreseen by Business Monitor International Report (BMI, 2015Q2). Pharmaceutical products have to be registered before any Marketing Authorization (MA) granted for the product following Law 127/1955. Although there are over 14,000 medicines registered in Ministry of Health, only 12,500 medicines are marketed and available in the market (MOH, 2015), due to challenges of production costs against the obligatory pricing and some of those are still in the registration pipeline, while others face challenges importing the active pharmaceutical ingredients and other chemicals used in production due to shortages of foreign currency cash flow. The pharmaceutical industry is composed of both local and multinational companies in addition to scientific offices, and toll-manufacturing<sup>1</sup> companies.

Medicines in Egypt are government-regulated and its price is controlled by law and ministerial decrees. Pricing is an essential step in the registration process of any pharmaceutical product. The pricing takes place through a pricing committee composed of experts from different disciplines.

Generic pharmaceutical products have to undergo a bioequivalence <sup>2</sup>test with the brand medicine prior to its final MA is granted. This test ensures that both generic and

---

<sup>1</sup> Firms that do not have its own manufacturing site. Instead, contracts with the existing factories to are approved to manufacture their products.

<sup>2</sup> Test used to assess two pharmaceutical products are bioequivalent; i.e.: pharmaceutically equivalent and their bio-availabilities after administration are similar to such a degree that their effects, with

brand medicines have the same biological characteristics and therapeutic potency as the brand medicine when administered to patients. All generic and brand medicines are analyzed for conformity against quality tests and registration dossier before its release to the market.

Patients have to pay out-of-pocket (OOP) for their medicines. The public health insurance covers only 58% of the population. Public hospitals adhere to a list of standard medicines that are publicly tendered and procured centrally. Patients have to purchase their medicines if not on the list of the public tender medicines. Private pharmacies are licensed by the MOH<sup>3</sup> and considered as the main legal outlet to sell medicines (i.e.: medicines are not sold in groceries or any commercial store other than the pharmacy<sup>4</sup>)

Although Egypt's pharmaceutical expenditure per capita is one of the lowest in the MENA region, it is still the largest market of pharmaceuticals among African and Arab countries (AmCham, 2015). Its infrastructure of pharmaceutical manufacturers, distributors, warehouses, and pharmacy outlets exceeds that of any other market in the region. However, the public health expenditure is still low compared to other countries.

Securing access to affordable medicines in Egypt requires considering the interests of all stakeholders involved in a pricing policy, namely patients and industry.

Affordability<sup>4</sup> comes at the forefront as a major determinant of access, given that patients are more likely to pay for their treatment OOP (Wanis, 2014). There is recent research done on medicine affordability in Egypt and its effect on access to medicines (HAI, 2014).

The affordability survey findings showed that when using generics, most standard treatments required less than 1 day wages upon purchasing 30 days treatment for NCDs. For treatment for hypertension, diabetes and hypercholesterolemia, then the patient would spend 2 to 7.8 days of wages every month to purchase medicines, depending upon the choice of medicine and product type (HAI, 2014). Some of the affordability findings and figures are shown in Annex.

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respect to both efficacy and safety, can be expected to be essentially the same. Pharmaceutical equivalence implies the same amount of the same active substance(s), in the same dosage form, for the same route of administration and meeting the same or comparable standards (Birkett, 2003).

<sup>3</sup> Mandated by Law 127/1955 -article(11)

<sup>4</sup> Mandated by Law 127/1955 -articles (32,37)

The Egyptian pharmaceutical market is expected to continue to grow. Reasons for growth include the increasing prevalence of non-communicable diseases, which require long-term treatments, consequently improving access is necessary step forward (AmCham, 2015).

## Chapter 1: Background

### Egypt Health Profile Egyptian Market Structure

The Arab Republic of Egypt is a lower-middle income country with a population size of 90.5 million (CAPMAS, 2016). The gross domestic product (GDP) of Egypt is USD 301 billion and there is 26 % of the population living under the national poverty line of USD 1.56 per day (CAPMAS, 2013).

The health system in Egypt is fragmented with multiple service providers (ISPOR, 2012). The Ministry of Health (MOH) lies at the center as the main service provider. Services are delivered through different establishments managed and overseen by the MOH, such as public hospitals, teaching (university) hospitals and hospitals belonging to the Health Insurance Organization (HIO), which is the public health insurance system. The coverage of HIO, however, is limited to about 58% of the population and covers only employees of the public sector (HIO, 2016)

Services in government facilities, including medicines, are provided either for free or against a small fee. Those who do not have insurance coverage can benefit from the Program for Treatment at the Expense of the State, which was initiated by the government with an independent budget (ISPOR 2012).

The number of pharmaceutical outlets is around 70,000 nationwide (Ministry of Health website, 2016).

### Pharmaceutical Industry

Pharmaceutical industry infrastructure and historical expertise has developed since the late 1930s (Holdipharma website, 2016). The number of pharmaceutical factories is 144, and the toll companies are around 1200 (MOH, 2016). These companies belong to three categories: (1) public sector companies; (2) local private sector companies; and (3) multinational corporations (MNCs). Public sector pharmaceutical companies operate under the umbrella of the Holding Company for Pharmaceuticals, Chemicals and Medical Appliances (HoldiPharma website, 2016).



Egyptian pharmaceutical market reached a value of EGP17.6bn (USD2.491bn) in 2014, and increased by 7.2 % ( 6.7% in local currency and 3.4% in US dollar terms) to reach EGP18.937bn in 2015 (Business Monitor International, 2015 Q2).

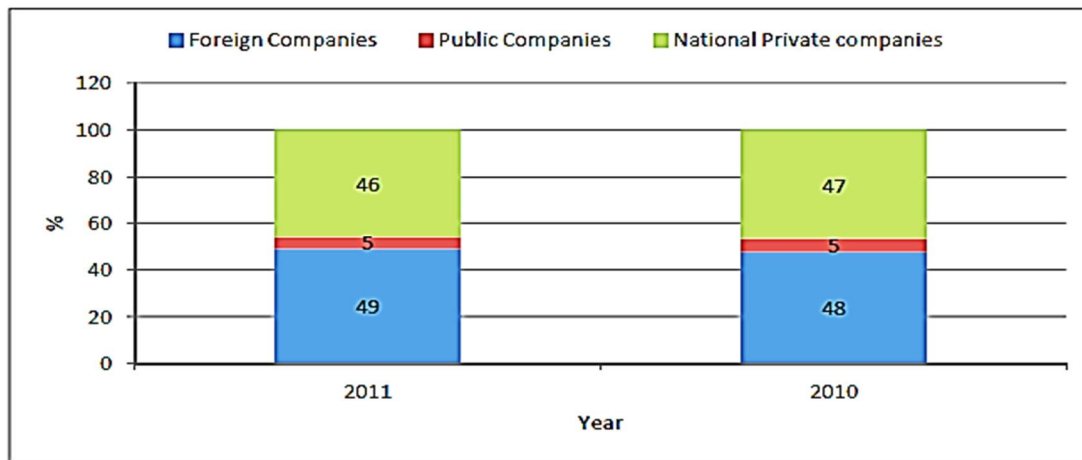
The market comprises both the private market (pharmacies and private hospitals) and the public market (government hospitals and healthcare centers).

The distribution of the sales value in 2011 according to ownership type shows that the market is relatively concentrated. In 2011, Herfindahl-Hirschman Index (HHI)<sup>5</sup> calculated by Abdelatif (2013) equaled 390.04, that was considered a relatively low concentration level of the market in big companies. That is pharmaceutical market has higher return on investments for big companies with higher market share, while it is low for small companies with lower market share.

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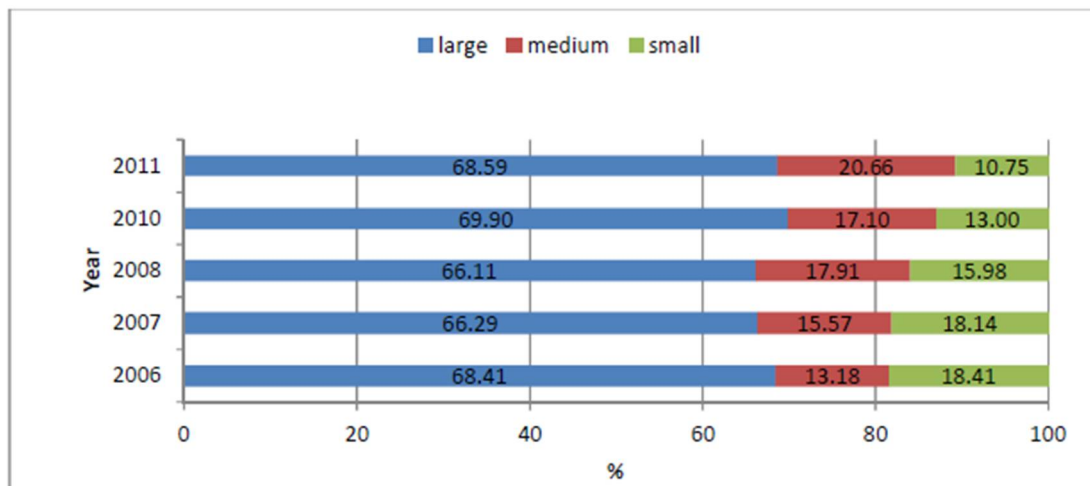
<sup>5</sup> HH1: is an indicator of the amount of competition among firms in industry according to their sizes. It is calculated by summing the squares of the market shares of the firms within the industry (usually limited to the 50 largest firms) then the result is proportional to the average market share. Increases in the Herfindahl index generally indicate a decrease in competition and an increase of market power, whereas decreases indicate the opposite.

**Figure 1: Pharmaceutical market share by company ownership comparison 2010-2011**



(Abdelatif, 2013)

**Figure 2: Pharmaceutical market share by company size (size by sales value)**



(Abdelatif, 2013)

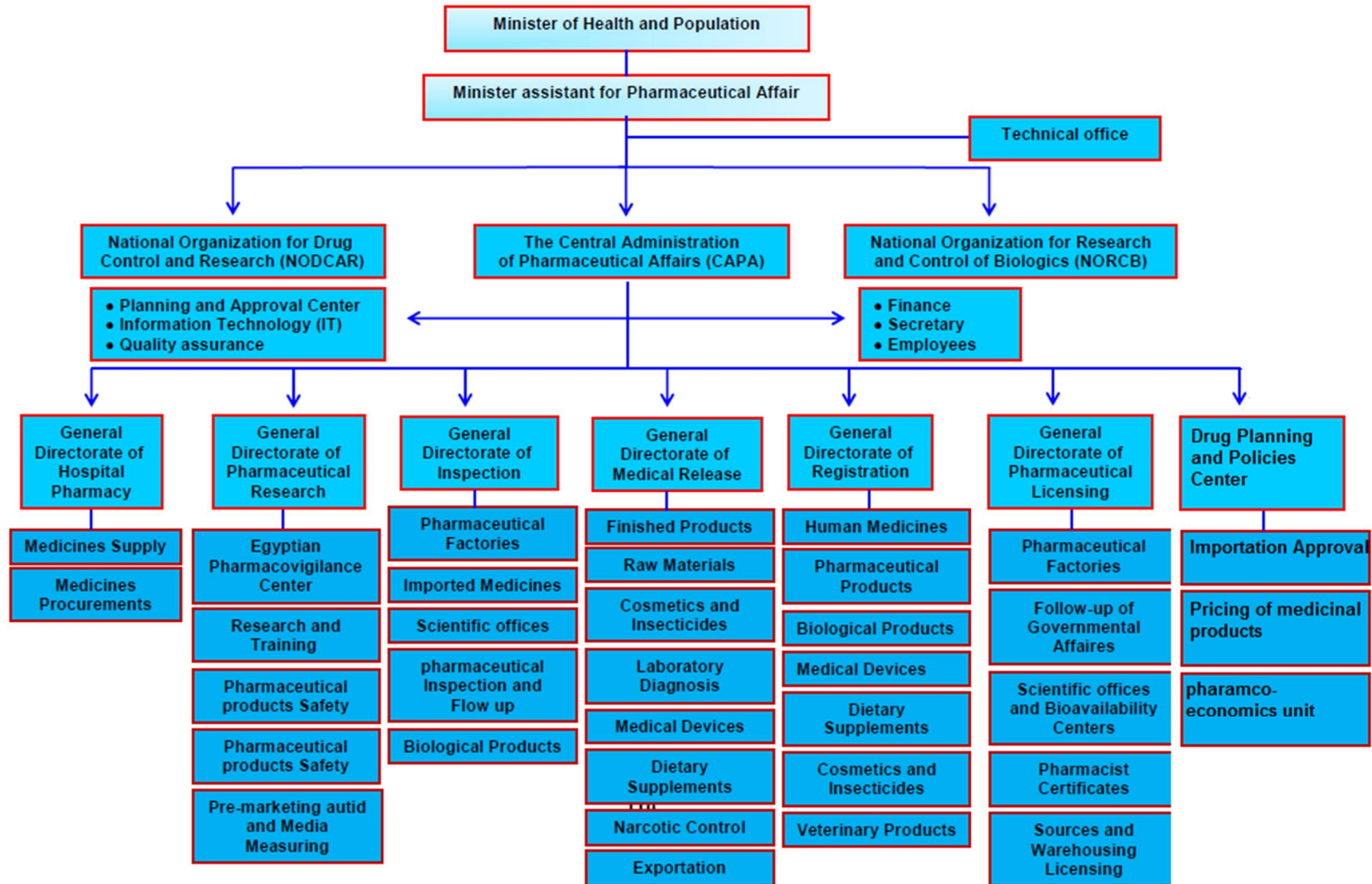
### Regulatory Framework

The national medicines policy for Egypt was last updated in 2005 (WHO, 2011), however there is no clear implementation or assessment plan for it.

The Egyptian authority responsible for control of medicines is represented in the Central Administration of Pharmaceutical Affairs (CAPA) under the Ministry of Health (MOH). CAPA comes at the forefront of drug regulation being mandated with critical responsibilities such as Registration, pricing of medicines, and inspection of pharmacies and manufacturing facilities. The CAPA hosts departments for

Registration; Licensing and Pharmacists' services; Inspection and Control; and Importation and Exportation. Figure 3 shows the organogram of CAPA where two of the main departments are the medicines registration and medicine pricing.

Figure 3: Central Administration of Pharmaceutical Affairs (CAPA) organization chart



### Medicines Registration

Registering medicines in Egypt is considered one of the first access barriers because of the involvement of multiple committees and application reviews prior to MA is granted. Egypt's public pharmaceuticals registration process on transparency score is 6.03 using the WHO methodology for measuring transparency (WHO, 2015). According to the report, low scores are related to problems of transparency in registration and pricing.

Registration of pharmaceuticals in Egypt follows what is called a "box" system. In the "box" policy, every dosage form (tablet, vial, syrup, suppositories, drops... etc.) of any active pharmaceutical ingredient has a definite number of similar products to be registered. The number of similar products for any API in specific dosage form is 12 products called "Box", and is composed of one brand product, and 11 generic products (10 locally manufactured generic products and 1 imported generic product).

The brand product is the medicine owned by one company that did research and development on the drug molecule and had its first clinical trials and approvals. The box registration policy was introduced in 2009 by enforcing the ministerial decree 296/2009 regulating the human medicines registration. The aim of this decree was to encourage the local investment by allowing 10 locally manufactured generic products to compete in the market and direct the market resources towards the neglected medicines (i.e.: empty medicines boxes) where no competing companies are investing their resources. Only one imported generic per box is allowed to be registered.

A bioequivalence test is required as one of the registration steps. It is considered as a proof of therapeutic equivalence to be provided in case of generic product. This test ensures its efficacy is within an acceptable range to the originator/brand. Acceptable ranges are usually between 80-125% of the Area Under-the-Curve<sup>6</sup> (AUC) in most guidelines. Products with low therapeutic index (i.e.: with high toxicity probability) acceptable ranges are between 95%-115%. (Abdelatif et al, 2013)

Currently ministerial decree 425/2015 is regulating the medicines registration and following the same "box" policy. It differs in some technical application through the

---

<sup>6</sup> A plot of concentration of drug in blood plasma against time. The area is computed starting at the time the drug is administered and ending when the concentration in plasma is negligible.

registration process enhancing the registration period and used parallel pathways instead of consecutive approvals.

While it is not guaranteed that all registered products will be available on the market because of the pricing policy applied, the decree 425/2015 cancels the registered medicine if not marketed after granting the MA by 18 months. . In case a product is registered, but gets priced too low which does not satisfy the producer, this will allow for ensuring the availability of an adequate number of products per pharmaceutical generics to replace the dropped medicine.

### **Medicine pricing policy in Egypt**

Historically, a strict obligatory pricing policy has been implemented with regulation of profit control, with the aim of making medicines affordable to the lowest socioeconomic segments of the population.

#### ***Pricing History***

Since the 1960s, medicine pricing was subject to special procedures to guarantee affordability. Pricing was mandated to the Egyptian General Foundation of Pharmaceuticals and Chemical Products, which took the full responsibility for the pharmaceutical system at the time (Wanis, 2014).

A special Pricing Committee was established by the Minister of Health to set prices or mark up for locally produced and imported pharmaceutical products.

Later, cost-plus and mark up regulation were put in place by two ministerial decrees in 1990 and 1991. This pricing system was based on economic cost. It specified profit margins for producers, distributors and pharmacists, and presented a detailed breakdown of the pricing process under direct costs, indirect costs, profit margin of the manufacturer, discount of expedited payment and distribution expenses, public retail price and revisions of product prices (MOH, 2016).

In 2009, decree 373/2009 distinguished between branded and generic medicines. Branded, or innovator, medicines refer to those primarily produced by MNCs; and they are either imported or produced locally under license, whereas generic medicines refer to locally produced off-patent medicines. Branded medicines were priced at 10

% less than the least price of a country where they are marketed. The decree provided a guiding list of 36 countries to use as reference countries. Generic medicines were priced at a mark down percentage of the price of the branded medicine. This pricing decree has been replaced by decree 499/2012.

***Current Egypt pricing policy***

Ministerial decree 499/2012 was issued in 2012 and still in place setting the pricing regulations.

The current policy adopts a combination of External Reference Pricing (ERP) and regulation of mark-ups and profit margins for the stakeholders in the supply chain. Reference countries used refer to their prices are the same list used in the decree 373/2009. Table (1) shows the list of reference countries used for external reference pricing in Egypt.

**Table 1: List of reference countries used in Egypt external reference pricing**

Price Certificate for Central Administration of Pharmaceutical Affairs , Ministry of Health, Egypt						
Company Name		Pack size				
Country		Ex-Factory in Country of Origin				
Product Name		Public Price in Country of Origin				
Generic name		CIF Price to Egypt				
Pharmaceutical Form		Currency				
No.	Country Name	Pack size	Ex-Factory Price	CIF Price/Currency	Public Price/Currency	Remarks
1	Algeria					
2	Austria					
3	Argentina					
4	Bahrain					
5	Belgium					
6	Canada					
7	Cyprus					
8	Denmark					
9	Saudi Arabia					
10	Finland					
11	France					
12	Germany					
13	Greece					
14	Holland					
15	Hungary					
16	Ireland					
17	Italy					
18	Japan					
19	Jordan					
20	Kwait					
21	Iran					
22	Norway					
23	Oman					
24	Portugal					
25	Lebanon					
26	Spain					
27	Sweden					
28	Switzerland					
29	U.A.E.					
30	U.K.					
31	Turkey					
32	Poland					
33	Sudan					
34	India					
35	Philippine					
36	Morocco					

According to the pricing decree 499/2012, price of the innovator product is determined according to the "lowest public" price in all countries in which innovator product is marketed. If the innovator product is marketed in less than 5 Countries, the price is determined according to either 1-comparative study, or 2- according to the lowest public price in all countries in which the innovator product is marketed.

The pricing of a Generic Product in this policy is as follows:

- The first five generic products are priced at 65% of the innovator product price.
- The rest of the generic products are priced at 60% of the innovator product price.



Within a given “box” of generic products, the pricing committee tends to strictly observe descending prices depending on registration date. The later the registration date, the lower the price given to the generic product. It is common to have long waiting lists of other products for registration in case a product dropped of the “box”. This happens in case a pharmaceutical company registers a product and does not market it for a period of 18 months.

Limitations of the ERP in Egypt pricing policy is that its use may involve incorrect choice of reference countries, i.e. countries with substantially different market structures or prices (e.g. a low-income country using high-income countries as the sole reference leads to inflated prices). Moreover, price information is not always available, and the available prices are often heterogeneous and often difficult to adjust them to obtain the required type of price. Finally, transaction prices are elusive – the prices that countries can access are often not real but virtual list/catalogue prices. True prices may be concealed for purposes such as rebates or risk-sharing arrangements, and sometimes launch delays and non-availability of new medicines.

Medicines prices contain the mark-ups that represent profitability margins for the pharmaceutical supply chain stakeholders, and in the same time affordability to patients.

### **Egypt pharmaceuticals and Intellectual Property**

Egypt is a member in world trade organization, and a signatory to the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement. This agreement protects the innovations by patenting the new molecule of drug for a period of time so that no other generic or equivalent medicine could be on the market. This mainly is to protect the free trade and the profitability of the innovator company.

Stages preceding the marketing and approval of new drug molecule involve the preclinical and Clinical trials on animals and humans that may range from 12 to 17 years. Filing of patents to protect the data is mandating all other WTO member countries to reject any goods that may violate the patent of the original product.

While medicine is a commodity used of public health protection, it was a great concern to be included under the TRIPS agreement. Doha rounds had successfully resulted in some flexibility to ensure protection of public health as will be explained in some later parts of this thesis.

Patents in some cases create monopolistic behavior for the innovator company world-wide especially after one incident relates to the HIV treatment (Kiddell-Monroe, 2014). In 2000, Médecins sans Frontières (MSF) innovated an HIV medicine that was priced at \$ 15,000 (Kiddell-Monroe, 2014). By implementing competition policies and epidemic state of African and Sub-Saharan countries, MSF decreased its price in response to more generic competition and allowed from 400,000 cases treated in 2003 to 1.6 million cases treated in 2006 (WHO, 2006). Consequently, the IP is a public health concern.

The IP issue in Egypt is handled by the Egyptian Patent office (EGYPO) which is the entity responsible for receiving, assessing and making decision on patent applications filed in Egypt (Egypt as other countries doesn't recognize patents granted in other countries, to be granted patent for your product protection you have to file a local application). Egypt had issued law number 82 in 2002 complying with the TRIPS agreement signed in 1995.

### Different pricing policies

The WHO had defined some governments interventions for regulations of prices.

Table2 illustrates some of these interventions

**Table 2: Definitions for pricing regulations as government interventions**

Policy/ intervention	Definition
<b>Regulation of markups in the pharmaceutical supply and distribution chain</b>	A mark-up represents the additional charges and costs that are applied to the price of commodity in order to cover overhead costs, distribution charges and profit. In the context of the pharmaceutical supply chain, policies might involve regulation of wholesale and retail mark-ups as well as pharmaceutical remuneration.
<b>Tax exemptions/reductions for pharmaceutical products</b>	There are two main categories of tax: direct tax, levied by governments on the income of individuals and corporations, and indirect taxes, added to the prices of goods and services and collected through the businesses that provide them. Direct taxes, along with social security taxes, generally make up about two thirds of total government revenue in high-income countries. In low-income countries, indirect taxes, on international trade or on the purchase of goods and services, are the major sources of government revenue. Policies might involve the reduction of taxes on medicines, or the exemption of medicines from taxes, particularly sales taxes.
<b>Application of cost-plus pricing formulae for pharmaceutical price setting</b>	Cost-plus pricing is a method for setting retail prices of medicines by taking into account production cost of a medicine together with allowances for promotional expenses, manufacturer’s profit margins, and charges and profit margins in the supply chain.
<b>Use of external reference pricing</b>	External reference pricing (ERP; also known as international reference pricing) refers to the practice of using the price of a pharmaceutical product (generally ex-manufacturer price, or other common point within the distribution chain) in one or several countries to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country. Reference may be made to single-source or multisource supply products
<b>Promotion of use of generic medicines</b>	Generic medicines are produced and distributed without patent protection. Promotion of the use of quality assured generic medicines is a method of managing pharmaceutical prices. The various approaches used include facilitated market entry of generics, generic substitution by dispensers, ERP, strategies to foster competition in the market, and schemes to encourage use of generics among providers and consumers.
<b>Use of health technology assessment (HTA)</b>	The International Network of Agencies for Health Technology Assessment defines HTA as “The systematic evaluation of properties, effects, and/or impacts of health care technology. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care. HTA is conducted by interdisciplinary groups using explicit analytical frameworks drawing from a variety of methods.” HTA in relation to pharmaceuticals encompasses evaluations relevant to price setting or pricing policies.

(WHO, 2015)

### *Reference Pricing*

An intervention usually set by governments to regulate prices of marketed medicines. As indicated by its name, a price for the medicine is set according to the price of the same medicine or similar one in another country or organization (Acosta, 2014).

Reference may be internal or external. In internal reference pricing, the medicine referred to is marketed within the same country. This pricing policy is used for reimbursement systems and for insurers' organizations.

In internal reference pricing and reimbursement policies, the reference price is set equal to one of the following (Verijens, 2010):

- 1) The lowest price defined in the cluster of medicines grouped together as in Australia,
- 2) The average of the prices of all medicines included in the cluster as in Netherlands,
- 3) The average of the lowest two prices in the cluster as in Denmark, The highest price generic drug in the cluster as in Portugal, and
- 4) by estimating regression model for all prices of medicines in the cluster as in Germany.

External reference pricing is setting the price of the medicine marketed in another country other than the intervening policy-setting country. In this case, the country is called reference country.

External Reference Pricing: The price of medicine in one country is set according to its price in another country. The country setting the price is called referee while the country with the established referred-to price is called reference country. Countries usually select other countries to refer to their prices based on some criteria. Being in the same geographic region, sharing borders, close socioeconomic characteristics, close income level, similar health systems. The price selected is usually the ex-factory price from the reference country. Mark-ups are then added according to the country policy in regulating the supply side margins (Espin et al, 2011). Some countries are usually used as reference based on the availability of price information, ease of access to public databases or lower prices globally.

This may well result in problems in the availability and affordability of some medicines in some countries, both within and particularly outside the OECD, unless

policy makers change pricing and reimbursement policies to adapt to the new market dynamic. (OECD, 2008)

In some countries, both internal and external reference pricing take place. When pricing a newly launched brand medicine in country for the first time, it uses the external reference pricing. Generic pharmaceutical then are priced for local marketing using the internal reference pricing. Margins and mark-ups are then added and adjusted for final price.

Table (3) shows the different adoption of ERP for pharmaceuticals and specific application to defined category of medicines (WHO, 2015).

**Table 3: Detailed External reference pricing followed in some countries; shows authority, products regulatence countries, and type of price used**

Country	Price setting	Products - ERP	Countries	Price used	Criteria	Sources of information
<b>Brazil</b>	Agência Nacional de Vigilância Sanitária (ANVISA)	On patent (Category I)	USA, Canada, Portugal, Spain, France, Italy, Greece, New Zealand and Australia	Ex-factory	Minimum	Websites;
<b>Czech Republic</b>	SUKL(State Institute for Drug Control)- maximum prices/reimbursement prices/ Health funds - price negotiations	Reimbursable	For pricing: Estonia, France, Italy, Lithuania, Hungary, Portugal, Greece, and Spain For reimbursement: all EU countries	Ex-factory	Average	Websites; Manufacturer
<b>Hungary</b>	National Health Insurance Fund Administration (OEP)	Reimbursable (new active substances)	Countries in the European Union and European Economic Area	Ex-factory	Minimum	Websites; Manufacturer
<b>Iran</b>	Pricing Commission	On-patent and imported	Greece, Spain, Turkey and the country of origin	Ex-factory and wholesaler	Minimum	Manufacturer
<b>Jordan</b>	Pricing committee of the Jordan Food and Drug Administration (FJDA)	All products	Selected European countries (UK, France, Spain, Italy, Belgium, Greece and the Netherlands), the export price to Kingdom of Saudi Arabia, and the country of origin	Ex-factory price of the reimbursed price	Median	Websites; Manufacturer
<b>Lebanon</b>	Pricing Committee - MoH	On- and off-patent products	Region: Jordan, Kingdom of Saudi Arabia, Kuwait, Sultanate of Oman, United Arab Emirates, Bahrain and Qatar. Comparative: France, England, Belgium, Switzerland, Italy, Spain and Portugal	All	Minimum	Manufacturer
<b>South Africa</b>	Pharmaceutical Economic Evaluations (PEE) Directorate	On- and off-patent products	Australia, New Zealand, Spain, and Canada	Ex-factory and import	Minimum	Manufacturer
<b>Sultanate of Oman</b>	Directorate General of Pharmaceutical Affairs & Drugs Control	All products	Gulf Cooperation Council (GCC) countries: Kingdom of Saudi Arabia, United Arab Emirates, Bahrain, Kuwait, and Qatar	Import price CIF (cost, insurance & freight)	Minimum	Manufacturer
<b>United Arab Emirates</b>	Committee - MoH	All products (some exceptions)	Country of origin and Gulf Cooperation Council (GCC) countries: Kingdom of Saudi Arabia, Kuwait, Bahrain, Qatar, and the Sultanate of Oman	Ex-factory and import	Minimum	Websites; Manufacturer

(WHO, 2015)

### *Index Pricing*

A pricing policy used mainly for reimbursement systems in which a group of similar medicines are priced according to the weighed-average of the therapeutic group of medicines. The reimbursement price is then defined and revised periodically to allow for improvement in the reimbursement price. The outlet is reimbursed for the indexed price when they dispense any medicine in the defined therapeutic group. This system allows for companies to lower its prices in a free market price to keep their market share of sales and to be on the top priority of dispensed medicines at the outlet. On the long run, reimbursement organization will revise index prices lowering the level to the actual dispensed medicines.

### *Maximum prices*

Also called ceiling price, in which a fixed price is set to secure pharmaceutical prices that are considered 'reasonable' for a given health system. There are different approaches to set the maximum prices: negotiated prices, price-caps, cost-plus, price comparisons to other countries or to similar products within the same country, or price-volume trade-offs (Mossialos 2004).

This is a cost containment measure that companies are allowed to choose any price below this threshold, described as price cap or price ceiling by the WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies Glossary (PHIS, 2016).

### *Profit regulation*

Mark-ups<sup>7</sup> can be regulated by the government or negotiated between the government and the companies, as under the Pharmaceutical Price Regulation Scheme (PPRS) in the UK (Borrell 1999). This can indirectly influence drug prices by setting profit limits. The PPRS is based on periodic negotiations between the Association of the British Pharmaceutical Industry and the Department of Health. It is reviewed every few years (PPRS 2009). If profits exceed a certain level, the company must reduce profits by cutting prices, delaying or restricting previously agreed future price increases, or repaying the excess profit to the Department of Health.

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<sup>7</sup> Margins of profit the company or the stakeholder has and reflect the Rates of return on the investment.

### *Stepped price model*

This policy is related to medicines with patents. Prices can be adjusted when patents expire. In Norway, a stepped price model was introduced in January 2005. In this model a maximum reimbursement price is set for drugs (both branded and generics). The maximum price is automatically reduced in steps following generic competition after patent expiry (Norwegian Pharmacy Association, 2008). The size of the price cut steps depends on the sales volumes prior to establishment of generic competition and the time since competition was established (Festoy 2008).

### *The competition policy pricing scheme*

In which the market is open and companies can freely price their medicines. Competition in this case should be protected by laws and regulations, e.g.: competition law and specialized organizations should be powerful enough to pursue such laws and enforce it. Not all countries can feasibly apply this scheme without health care coverage and reimbursement system, and adequate independent and functioning jurisdictional system in place with powerful enforcement authorities in cases of violations. In this case the cost for anti-competition measures can be high regarding the patient health and availability of medicines. (Hawkins, 2011)

### *Other pricing policies*

These may include price negotiations, volume-based pricing, procurement and rebate policies.

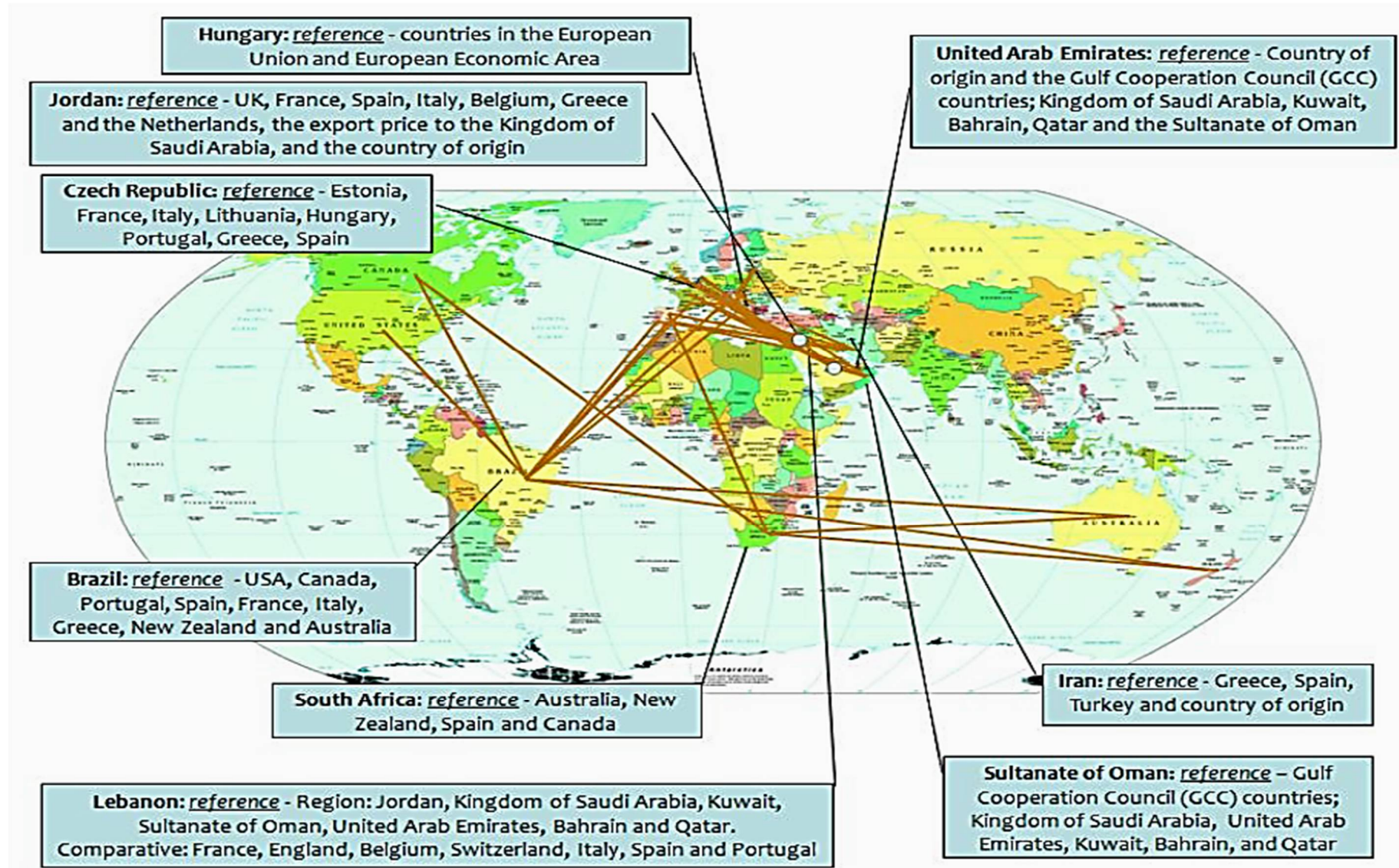
When negotiating the price, several considerations can be taken into account: costs of products, prices in comparable countries, therapeutic value of the product, evidence of clinical effectiveness and safety, and price-volume arrangements.

Under a price-volume arrangement, the agreed drug price is based on a forecast volume of sales. If the actual volume exceeds the forecast, the drug price usually has to be lowered. Pricing regulation may apply to initial or posterior prices once products are marketed, and can be based on prices for the same product in other countries or on the costs of similar treatments for the same indication (Espin, 2007).

Reimbursement decisions and pricing for new drugs can also be based on economic evaluations of the new treatment compared with existing options (Espin 2007).



Figure 4: Map showing countries using ERP and their reference countries



(WHO, 2015)

## Socioeconomic Factors

Egypt has strong socioeconomic class stratification, with large income gaps. This stratification is manifested in housing and sanitary conditions, literacy levels, health awareness, working conditions and, accordingly, types of prevalent diseases. Social implications of the above economic factors can act as barriers to accessing medication (Wanis, 2009).

Egypt Gross Domestic Product (GDP) was worth 301.5 billion US dollars in 2014. The GDP value of Egypt represents 0.37 % of the world economy (Trading and economics website, 2013). Although Egypt GDP per capita is USD 3,198 in 2014 (WB, 2016), it is not indicative of the average income level, as there are 26.3 % under the poverty level (WHO, 2002). There is 32.2% of rural population living at the national poverty line<sup>8</sup> (WB, 2010). There is noticeable bias in resource allocation towards higher income groups.

Egypt consists of twenty seven governorates; five of which are urban; Egypt, Alexandria, Suez, Ismailia, and Port Said. The remaining twenty two governorates are characterized by urban and rural areas. Nearly 40% of Egyptian population lives in urban areas (Figure 5: Egypt Rural population as percent of total population); Cairo and Alexandria are among the world's most densely populated.

Government healthcare services tend to be through big programs, which unintentionally favor urban populations. It has been argued that “access to medical services in rural areas is limited and selective” in developing countries (Bapna et al., 1996).

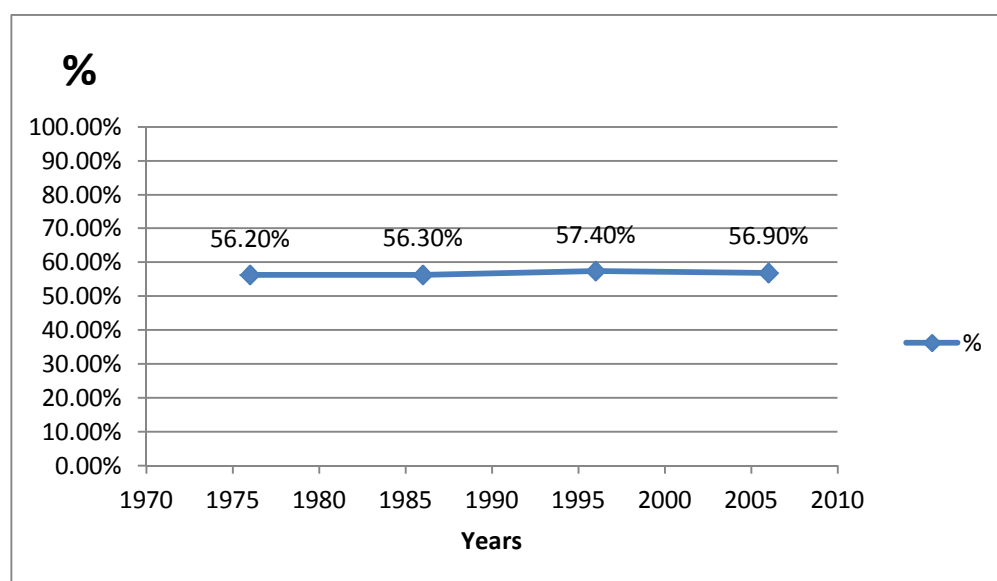
Medication costs constitute around 53% of average health care expenditure (CAPMAS, 2013) shown in Figure 7: Percentage distribution of Expenditure on Healthcare 2012/2013 . With inadequate insurance coverage and high out-of-pocket health expenditure, income level becomes a major determinant of access to medication. Rural areas are at higher risk of facing inadequate access to healthcare due to their higher percentage of poverty.

Adult literacy rate is 61%; illiteracy is particularly high in rural areas (WHO, 2005). Lack of health awareness, negligence and reluctance to seek medical advice indirectly influence access to healthcare services and, accordingly, necessary treatment.

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<sup>8</sup> Poverty line was defined by CAPMAS in 2013 as EGP3900 annual income (CAPMAS, 2013).

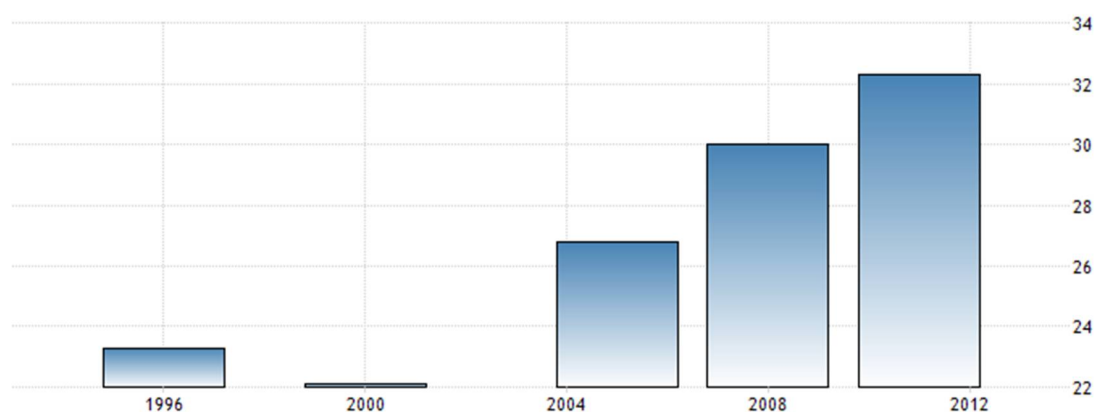
**Figure 5: Egypt Rural population as percent of total population**



(CAPMAS, 2013)

While the poverty headcount rate in rural population was around 32% of rural areas in 2012, the rural areas constitute more than 67% of poverty that represent more than quarter, 26.3%, of the Egyptian population. That is quarter of Egypt population are poor and more than two thirds of this poverty lies in rural areas.

**Figure 6: Poverty percentage of rural population**



(Trending Economics, 2016)

**Table 4: Percentage of poor among socioeconomic areas in Egypt**

Unit : (%)

Item	2012/2013	2010/2011
Urban governorates	15.7	9.6
Lower Urban	11.7	10.3
Lower Rural	17.4	17.0
Upper Urban	26.7	29.5
Upper Rural	49.4	51.4
Boundary governorates	24.2	36.9
<b>Total Egypt</b>	<b>26.3</b>	<b>25.2</b>

(CAPMAS, 2013)

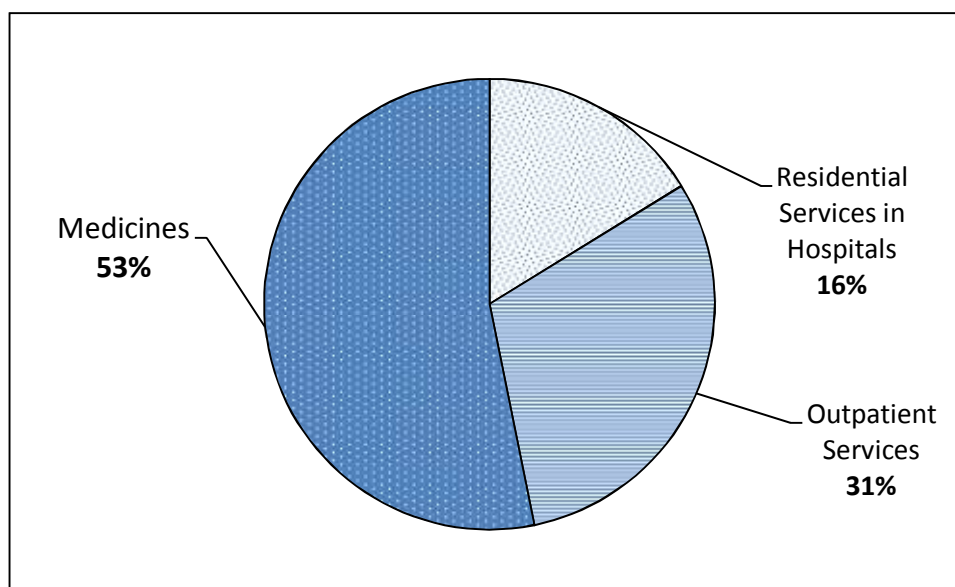
CAPMAS published the household survey for 2013 that showed expenditure classes distribution. It was amazingly found that the highest spending class of EGP12,000/person or more annually is 6% of the population. The urban population has 11.8% lies in this high spending category, while only 2% of rural population are there.

The highest percentage of population spend EGP4,000– EGP5,000/ person annually. On the contrary, population had 38% and 31% of rural and urban residents respectively are located in this class. (CAPMAS, 2013)

The expenditure items classification in 2013 showed that the individual spending on the healthcare item was higher in rural population, 10.1%, relative to the urban population, 9.5% (CAPMAS, 2013). This shows the higher burden for health care costs in the rural areas in addition to the higher poverty levels indicated in lower expenditure classifications.

The segmentation of health care expenditure shows that 53% are spent on medicines, while the rest is used for physician visits and inpatient care.

**Figure 7: Percentage distribution of Expenditure on Healthcare 2012/2013**



(CAPMAS, 2013)

As poverty prevails more in rural areas, as the income of the rural population increases, they will be in a better position to demand better health, education and other social services and pay for them in the longer run. What is obvious, therefore, is that being poor is very much a characteristic of residing in rural Egypt and thus having less access to public goods and services

Meanwhile, about 57% of the total population in Egypt lives in rural areas, where poverty prevails. About 70% of the poor and very poor live in rural areas. Within these realities of the Egyptian economy, enhancing sustainable agricultural and rural development as a means to reduce poverty and food insecurity within the expected climate changes is a prerequisite for sustainable social and economic development and hence should be considered as a social and political priority for Egypt (Handoussa, 2010).

**Table 5: Estimated Household distribution according to wealth index**

Weather Index	Place of Residence		Total %
	Urban%	Rural %	
Lowest	6.8	30.8	20
Lower Middle	11.7	26.5	19.8
Middle	17.2	22.6	20.2
Upper Middle	27	14.3	20
Highest	37.3	5.8	20
<b>Total</b>	<b>100</b>	<b>100</b>	<b>100</b>

(USAID, 2010)

**Table 6: Percentage distribution of annual individual consumption by main expenditure group and socioeconomic area of residence**

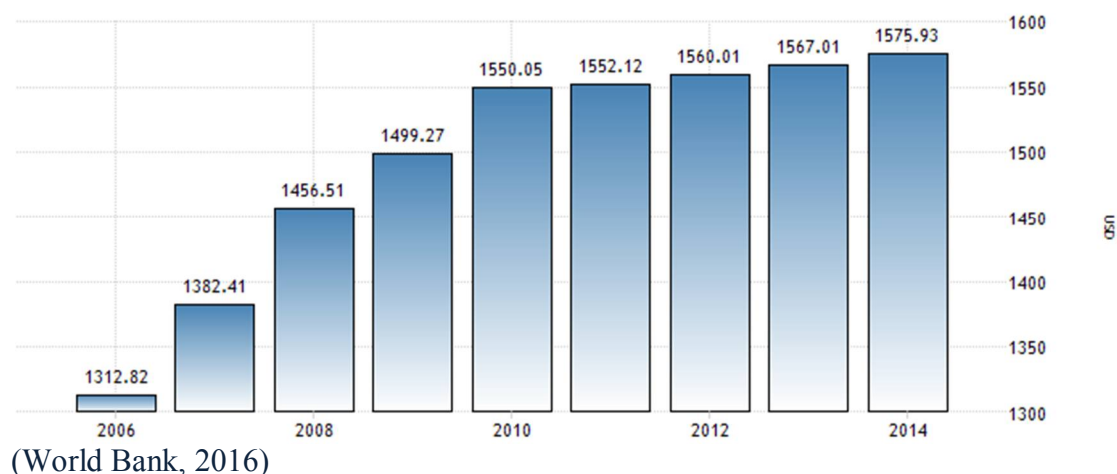
Unit : (%)

Expenditure Group	2012/2013			2010/2011		
	Total	Rural	Urban	Total	Rural	Urban
Food and drink	36	39.7	32.5	39.9	45	35.6
Beverage and Tobacco	3.3	3.6	3.1	3.4	3.8	3.1
Clothing and textiles	5.7	6.2	5.3	5.3	5.5	5
Housing	18.6	17.2	19.9	18	16.9	18.8
Furniture and maintenance	4.3	4.4	4.1	3.9	3.8	4
<i>Healthcare services</i>	9.8	<b>10.1</b>	<b>9.5</b>	8.1	8.3	8.1
Transport	5.8	4.7	6.9	5.3	3.8	6.6
Communication	2.7	2.2	3.3	2.5	1.9	3
Entertainment	2	1.7	2.2	2.2	1.5	2.7
Education	3.7	2.3	5	3.9	2.2	5.4
Hotel and Restaurants	3.6	3.1	4.1	3.5	3.2	3.8
Miscellaneous goods and services	3.3	3.1	3.4	2.9	2.7	3
Total Annual Household Expenditure	100	100	100	100	100	100

(CAPMAS, 2013)

Adequate health care coverage and insurance is basic need that the State guarantees for all citizens (under the latest Egyptian Constitution, article 18). Article 238 of the constitution enforced the health care budget to reach 3% of the GDP when it used to be 1.6 % of GDP in 2013/2014 fiscal year.

**Figure 8 : Egypt GDP per capita**



## Non-Communicable Diseases

Non-communicable diseases (NCDs) are a global health crisis. By 2030, 75% of the world's deaths will be caused by cancer, diabetes, CVS and lung disease. Not only are NCDs a global health crisis, they also reveal a crisis of global health inequality: most of NCD deaths reported worldwide occur in low- and middle-income countries (LMIC), (WHO, 2008).

The purpose of this study acquired its importance from the highest burden NCDs in Egypt. NCDs account for 82% of deaths and 67% of premature deaths in Egypt (WHO, 2016). NCDs with highest burden in Egypt are Cardiovascular (CVS) diseases, Diabetes Mellitus (DM), and respiratory (Asthma,COPD), and Renal diseases.

NCDs kill 38 million people each year globally. Almost three quarters of NCD deaths - 28 million - occur in low- and middle-income countries (LMIC). Sixteen million NCD deaths occur before the age of 70; 82% of these "premature" deaths occurred in low- and middle-income countries (LMIC), (WHO, 2016).

Cardiovascular diseases account for most NCD deaths, or 17.5 million people annually, followed by cancers (8.2 million), respiratory diseases (4 million), and diabetes (1.5 million). These 4 groups of diseases account for 82% of all NCD deaths (WHO, 2016).

In Egypt, the aggregate labor supply is around 19% below its potential, driven by lost employment and reduced numbers of hours worked by those reporting chronic conditions, implying an overall production loss of roughly 12 percent of the country's GDP (Rocco et al, 2011).



## Research Question

According to the World Health Organization, access to medicines is measured by two factors, affordability and availability (WHO, 2003). Linking the pricing policy; affordability on the one hand, to the socioeconomic influences; availability on the other hand, will be an important milestone for setting any pharmaceutical regulation. Affordability and prices survey was conducted in 2013 and found that mostly all medicines on the EML List for chronic diseases are affordable (HAI, 2014)

Non-Communicable Diseases (NCDs) affect adults in their productive years, require long term treatment and often cause disability. They can have more severe economic consequences for the individual and his or her family,—including decrease or loss of household income, impoverishment, loss of savings and assets, and reduced opportunities—than other illnesses. While the burden of NCDs is rising, it can constitute a major health challenge of access to affordable NCDs medicines.

From a social equality perspective, all socioeconomic classes should have the same privilege of access to brand medicines as well as its generics. The prescribing behavior of the physician may be influenced by the socioeconomic class and geographic location of the patient due to the difference in prices of the brand and generic medicines.

The study of availability of both brand and generic medicines will certainly reshape the policy for registration, pricing, and pharmaceutical trade; import and export.

This research will reveal some of the market behavior in different socially distinct geographic areas. To what extent of urban and rural conditions affect the medicines supply. The null hypothesis for the research is "in comparison to Brand medicines, their generics are equally available in both urban and rural areas". The alternative hypothesis is "In comparison to Brand medicine, their generics will be more available in rural rather than urban areas". Some actions may be required for allowing equal availability of brand and generic pharmaceutical products.

With extensive review of the literature, and up to our knowledge, there is no Egyptian study had been done before for the analysis of the urban and rural determinant for market supply of generic and brand medicines in Egypt.

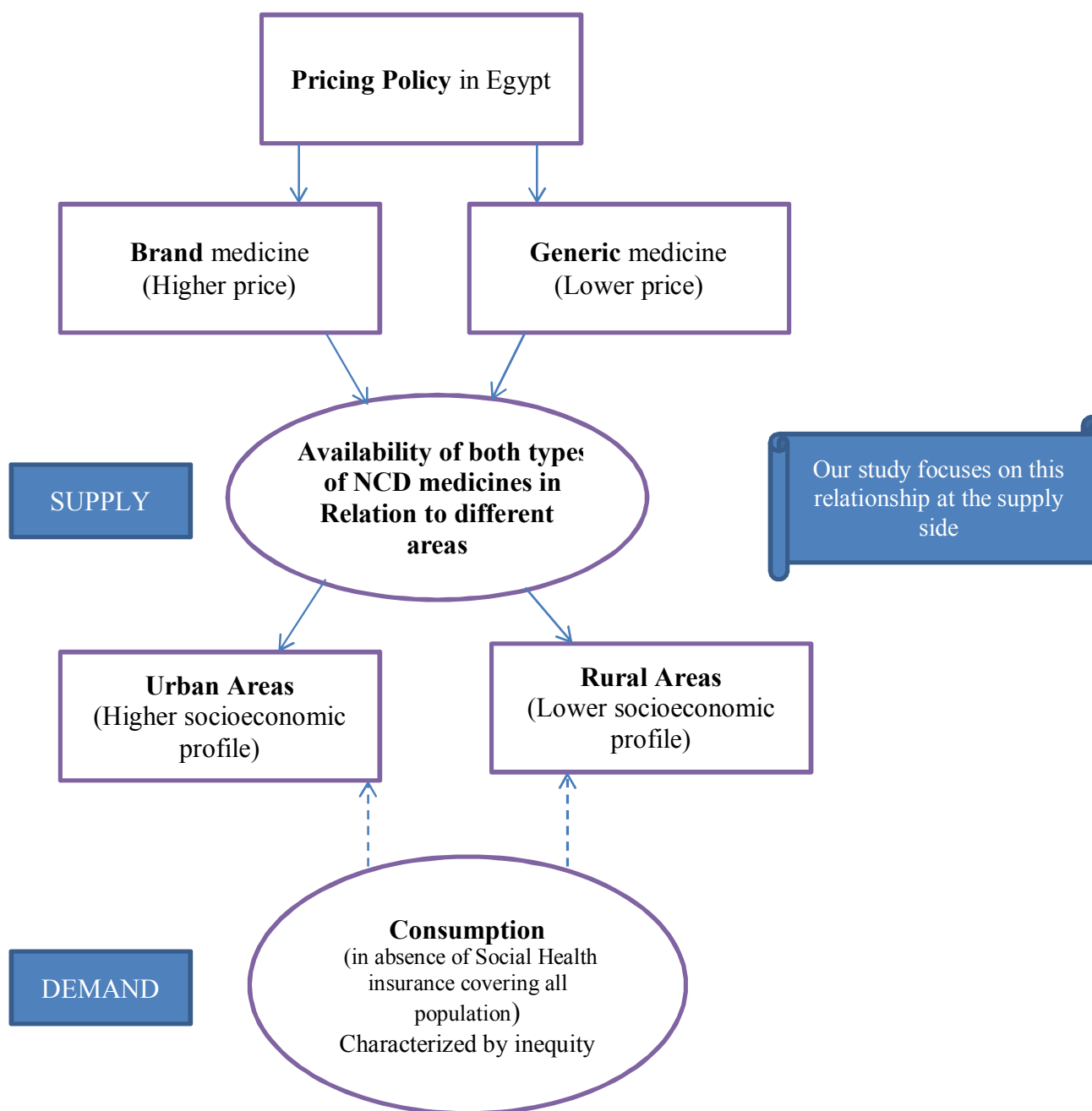
## **Conceptual Framework**

This research paper investigates the relationship between the pharmaceutical supply of the medicine types, and the rural and urban areas where patients reside. The association has been studied before in different countries other than Egypt. Prior studies were done considering the consumption perspective; i.e.: the demand side of the market. Supply side was not investigated in most studies. While firms with brand products have higher prices usually target those higher socioeconomic classes, rural areas are targeted by generics suppliers. Deliberate choice of either brand or generic by patients may be absent due to the role of supply side as a determinant of the market consumption.

While Acosta et al (2014) and Stargardt (2009) illustrated that reference price for reimbursement organization does not affect the patient health at all, it only affect the other competitor companies to lower their prices, Khan et al (2015) showed that 60 % of low income household in 18 LMIC cannot purchase the medicines not only due to the financial constraint but also due to several socioeconomic determinants where we will investigate the solid relation between the supply and urban/rural preference of the outlet. And most important, Skipper et al (2015) concluded that patients socioeconomic characteristics differ in probabilities of choosing brand product medicines by 2.9% higher for those employed patients rather than unemployed.

As pricing policy of pharmaceutical differentiates between brand medicines and its generics, brand medicines have higher prices than its generics. Suppliers will then be able to market their medicines to the urban areas having higher socioeconomic context rather than rural areas with lower socioeconomic profile. The relationship between the brand/generic and price is already established. So, we will study the relationship between brand/generic medicines with its availability/supply in urban/rural areas in Egypt as a result of the pricing policy followed as shown in Figure 9: Conceptual framework for this research.

**Figure 9: Conceptual framework for this research thesis**



## Chapter 2: Literature Review

While most studies in the literature controlled for very comprehensive set of political and socioeconomic covariates (Vatter et al, 2003). Empirical studies of the socioeconomic impact on consumption of brand and generic medicines have not reached consistent conclusions.

For all drugs in Belgium, the reference price is based on a simple reduction in the ex-factory price of the brand drug then increased by the distribution and pharmacy margins to obtain the public price (Farfan-Portet et al, 2012).

In a study that is relevant to our research, one of the important findings that Farfan-Portet et al (2012) had is the positive relationship between the use of a generic drug and a lower socioeconomic status. The characteristics of the drugs may also be important; whether acute diseases requiring treatments for short time periods, or drugs for serious complex and chronic conditions requiring the prolonged treatment periods.

Farfan-Portet et al (2012) recommended that for mitigating the socioeconomic determinant in the choice of brand versus generic medicine, that physicians should be aware of the minimum percentage of low cost prescriptions. A color code was introduced to the National Drug Information Center to increase awareness of the excess prices paid over the reference prices set by the reimbursement/insurance organization in addition to publishing an easily accessible price comparisons for all drug groups on the website of the Information Center, and the third-party payer (the National Institute for Health and Disability Insurance -RIZIV/INAMI)

Switching between brand and generic medicines is not allowed in Belgium for pharmacists except in case only when the prescription is written using the International Nonproprietary Name (INN) of the drug, then pharmacists are allowed to deliver a low-cost drug. It is only 7% of prescriptions that were written using INN in 2009. (Farfan-Portet et al, 2012).

Only four papers analyzed the impact of reference pricing according to the socioeconomic and patient characteristics (Verijens et al, 2010). Verijens et al (2010)

analyzed the reference price system in different countries based on three major attributes to which fundamental use of the system differs. These three objectives were what medicines are to be covered under the system, which price used as reference, and finally incentives for the use of lower cost medicines.

While New Zealand, Australia and Netherland apply the grouping of Anatomic Therapeutic Chemical Classification<sup>9</sup> (ATC-4) level for reference price (that is the pharmacologically equivalent molecules are grouped together), Denmark, Portugal , France and Spain apply the ATC-5 level grouping (all medicines have the same active pharmaceutical ingredients; brand and generic) of reference price application. Italy, Hungary and Canada apply the reference system to cluster grouped according to ATC-3 level (the therapeutically equivalent while pharmacologically different molecules are grouped together)

While reference price system contributes to the improvement in health expenditure savings in British Columbia, Canada, patient socioeconomic characteristics were not different when using the health services. RPS however, induced the lower socioeconomic patients for tendency towards the use of reference low cost pharmaceutical products rather than higher socioeconomic patients (Schneeweiss et al., 2003).

In one other important working paper, Rischatsch and Trottmann (2009) showed the relationship between patient deductibles under their insurance coverage to the use of generic medicines. The higher the deductible, the higher the tendency for using lowest cost generic medicine. Patients with higher socioeconomic background have lower sensitivity to the higher price of brand medicines because of the lower marginal utility of their income.

Skipper et al (2015) found that socioeconomic characteristics of both patients and doctors to have low explanatory power. Patients socioeconomic characteristics differ in probabilities of choosing brand product medicines by 2.9% higher for those

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<sup>9</sup> Pharmaceutical coding used for classification system: It divides drugs into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics. Each bottom-level ATC code stands for a pharmaceutically used substance, or a combination of substances, in a single indication. One drug can have more than one code

employed patients rather than unemployed. Introduction of generics and their inherent impact on the price of treatment seems to explain roughly one third of the variation in drug choice (Skipper et al, 2015).

Khan et al (2015) found that in Low- and Middle-Income Countries (LMIC) there is risk of negative health outcome due to the decreased access and availability of medicines used in cardiovascular conditions. They showed that 60 % of low income household in 18 countries cannot purchase the medicines not only due to the financial constraint but also due to several socioeconomic determinants as health literacy and general awareness, and provider competency.

Schneeweiss et al. (2002) found that compared to high income patients, those on low and middle income were more likely to switch to the less expensive drug (the reference drug) or to switch from the expensive antihypertensive drug (having a reference supplement) to another antihypertensive therapy. However, the authors also mentioned that before and after the introduction of the RPS stopping any antihypertensive treatment was more likely for low income patients.

Schneeweiss et al. (2003) analyzed the use of dihydropyridine calcium channel blockers; an antihypertensive medicine, and the use of health services after the introduction of the RPS. They found that low-income patients had on average a higher probability to switch to the no-cost dihydropyridine (reference drug) or to switch from the expensive dihydropyridine drug (having a reference supplement) to another antihypertensive therapy (nitrates). Patient characteristics were found not to be associated to the impact of the RPS on physician visits, hospitalization and admission to long-term facilities.

Ibrahim et al (2012) recommended that generic medicines used for hypertension should be available in the public primary care level and that scrutiny should be followed to ensure the quality control of their dispensing and efficacy in relation to other drug interactions.

Recent studies searching for the effect of pricing mechanisms and reimbursement policies on people's health and adverse events are lacking. Most internal reference pricings and index pricing used for the lowering of the medicines cost to insurers and reimbursement organizations (Acosta et al, 2014). The internal reference pricing largely indicated savings on health spending and shift towards the reference-priced medication, whether it is brand or generic. Mostly, pharmacy outlets tend to dispense the generic medicines within the set group of medicines under the index pricing scheme to maximize the benefit of reimbursement (Acosta et al, 2014).

While some countries utilize the internal reference pricing for pharmaceuticals, they do not set prices out of the reimbursement systems.

In terms of financial accessibility, the internal reference price system in Belgium does not impose an unbalanced financial burden on low-income patients. However, some patients are still bearing the cost of using brand medicine when a cheaper alternative is available. Moreover, there are prescriptions entailing a reference supplement. This is particularly important in a system of generic reference pricing with narrowly defined clusters where potential differences in clinical effectiveness of generic and brand drugs can be regarded as negligible (Farfan-Portet, 2012)

Perception of equivalent generic and brand medicine is important key concept for switching to any of both. Kohli and Buller (2013) studied the consumer purchasing pattern for generics and brand Over-The-Counter (OTC) medicines in US. The study concluded that the main factor for the purchasing pattern for OTC medicines is the medicine price. Lower price OTC medicines were believed by 90% of participants to be of equal quality and safety as long as it undergoes the FDA approval.

In Egyptian pharmaceutical regulatory system, bioequivalence was introduced as key step in medicines registration in 2008 (Abdelatif et al, 2010). This test ensures that both brand and generic medicine of the same active pharmaceutical ingredient have the same efficacy, potency and bioavailability within the acceptable standard range.

In France, pharmacists have the financial incentives to dispense generic medicines (Venjens, 2012). Switching between generic and brand is a pharmacist right and patient consent is required except in cases prohibited by the physician when the medicine has a narrow therapeutic index or when guidelines state that medicine to

begin with is to maintain on for the course of treatment. This might be applicable to NCD medicines except for those with narrow therapeutic indices as mentioned. (Venjens, 2012). He also claimed that implementing reference price system was not followed in reduction of branded pharmaceutical products prices.

Although the quality of both brand medicines and its generics are controversial, Badjatya et al (2013) claimed that once USFDA approved a generic drug it means that this generic had undergone rigorous evaluation procedure and mentioned that

*"The USFDA requires that generic drugs work as fast and as effectively as the original brand-name products", and also "Generic drugs have same onset of action, mechanism of action, and release profile to brand drugs"* (Badjatya et al, 2013).

Vaithianathan et al (2015) concluded that for some selected medicines, a set of analytical tests done verifying the appearance, identity, assay, impurity, uniformity of dosage units, disintegration, dissolution, friability, and loss on drying of a brand medicine and its generics. These market surveillance results indicate that all brand and generic passed all tests and showed acceptable pharmaceutical quality and low biopharmaceutical risk.

On the one hand, supporter of equivalent quality of both brand and its generics claim that any regulatory authority would ensure the equal quality for both medicines. On the other hand, Yang et al (2012) revealed that not all tests performed for comparison between a brand and its generics is successful. Dissolution and assay tests for both medicines may reveal the different formulation of both medicines and, hence, different onset of action. However, the importance of exact results are not required in most cases as long as therapeutic indication is addressed unless the medicine has a narrow therapeutic index and higher toxicity margin that requires extra tests and verification of the equivalent therapeutic actions (Yang et al, 2012).

The USFDA defined the bioequivalence for generics as to have no significant difference in the rate of bioavailability of the drug molecule at the site of action for both brand and its generic (FDA, 2003). While acceptable range of bioavailability is 20 percent below and 25 percent above; that is 45 percent variability between brand and its generics. Then, as referred to above the medicines with narrow therapeutic index have to be closely monitored when releasing copies of brand medicines (generics) into the market.



Gazzili et al (2010) concluded that reference price tend to reduce the branded medicine prices in free markets. When firms with brand pharmaceuticals do not respond to the reference price, they allow more market share for generics. They also concluded that there is no association between the reference price system (therapeutic reference) and the health outcomes. That is no socioeconomic profile was considered.

Abdelatif et al (2013) recommended that Egyptian pharmaceutical market should be more open by cancelling the box-policy registration to allow more access to medicines. It is the market-derived not government-enforced decision for any company with new-entry medicine, whether brand or generic. However, securing market supply of pharmaceuticals is considered as national security issue.

Simoens (2009) elaborated that pharmaceutical pricing in Poland is not mandatory for firms that are not willing to be included on reimbursement system of the country. Patients do not have the incentives to shift from brand to generic or the vice versa except for reimbursed reference price. Patients pay their co-payments that exceed the reference prices defined by the reimbursement system and no preference for purchasing either brand or generic once the physician had prescribed the medicines.

Some countries, such as France and Italy, regulate drug prices directly through price control; others, such as Australia, use Pharmaco-economic (PE) analyses and reference pricing to determine the prices of drugs subsidized by the government (Danzon, 2000).

Germany and Japan control prices indirectly through limits on reimbursement under social insurance schemes (Danzon, 2000). In The Netherlands, the government introduced reference-pricing system in 1991, and wholesalers were forced to lower their prices by an average of 20% in 1996 (Gier, 2003). Pricing regulations also seem vital, as in many Latin American countries “free schemes of drug prices” have not proved effective as a cost containment mechanism. In Guatemala and Peru, prices have increased over and above the exchange rate or the consumer price index, and in Bolivia the practice of the free market concept has not yielded any benefits (Sarmiento, 1995).

In India, essential drugs cannot cost more than twice the cost of production, and the maximum retail price and local taxes must be included in a drug's final printed price (Kumar, 2004). This model follows the “cost-plus pricing” where the prices are negotiated between the manufacturer and the national authority, based on raw material costs, production costs, marketing costs, and a reasonable allowance for profit.

The entry price for the new drug in the market is an important factor determining the other generics prices later on. In Germany, prices are anchored at certain level. Although not an external reference price- following country but their prices are referred to by other potential markets. This explains why high prices in Germany are maintained nevertheless the local market is not influencing the price decrease. It is mainly to avoid harming the prices in other markets (Mueller et al, 2013)

Stargardt (2009) illustrated that reference price for reimbursement organization does not affect the patient health at all, it only affect the other competitor companies to lower their prices including those brand products if included in the reimbursement system.

Similar study was conducted in Sri Lanka showed that availability of brand products over private pharmacies is 26% (Dabare et al, 2014).

Anggriani et al (2014) conducted a study for generic and brand availability. They concluded that regulation of medicine prices through generics policy in Indonesia promotes the lowering of generics prices while branded products prices are not regulated.

Not only governments have to measure their efforts for improving access to medicines, but also private Research and Development (R&D) companies are stakeholders. Consensus is required amongst those pharmaceutical companies supplying medicines used for treatment of diseases of worldwide concern.

Kyle (2006) indicated that market access is not a function of the government only. It is a shared substantial effect of both the local market and the company characteristics and willingness to launch its product in certain market. Kyle concluded that price controls have an influence on delayed launch of R&D companies in other foreign market. While shared borders and language is preferably enhancing the quick launch

of the new pharmaceutical product, it remains the company tendency to provide treatment for certain population and profitability rather than enhancing access to medicines in a global context.

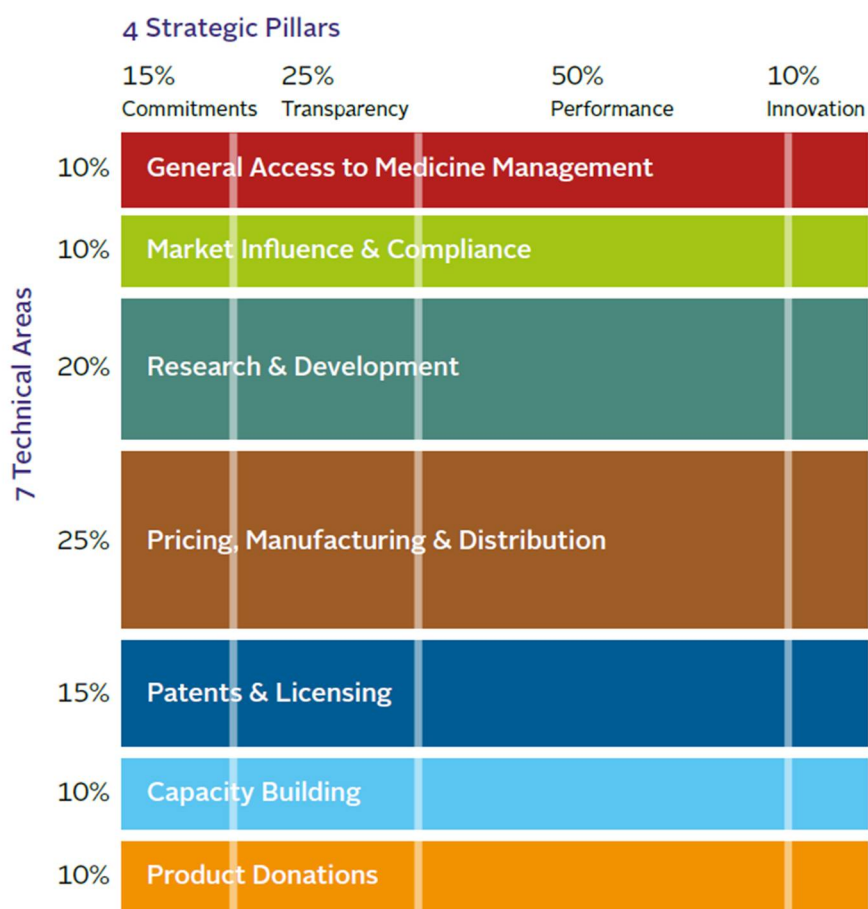
Panchal et al (2012) discussed the brand loyalty and the perception of the brand versus generic medicine in Indian pharmaceutical market. While health authorities and reimbursement systems in India prefer the lower priced generic products for the savings impact on health spending, the brand loyalty and perceived quality have major influence on use of brand medicines rather than generics in India.

Companies currently spend one-third of all sales revenue on marketing their products - roughly twice what they spend on research and development (WHO, 2016).

Communicating the brand pharmaceutical products by R&D company as superior to any generic medicines has been a social determinant in affecting the pattern of thought leaders use of brand pharmaceutical products. The prescribing behavior also can be determinant in brand equity transferred from physicians to consumers. Panchal et al (2012) concluded that price was not studied as the only factor in determining brand versus generic consumption, the brand loyalty, awareness, and quality perception had major concern related to brand equity related to generics.

The access to medicine index is an indicator that is based on the measurement of technical areas and performance indicators in low- and middle-income countries (LMIC) around the world. Its measurement covers variety of diseases, of these cases that it measures there are medicines for 14 non communicable diseases are measured for their access. The index is mainly focusing on the top 20 R&D pharmaceutical companies.

**Figure 10: Accessto Medicines Index indicators and areas of measurement**



(Access to Medicine Index, 2016)

We can obviously observe that one quarter of technical areas that influence access of pharmaceutical companies' medicines is the pricing. While on the horizontal plane there is the three quarters (75%) related to performance and transparency combined.

So, for any company to launch its medicine, e.g.: NCD medicines, it has to make sure that pricing is transparent and the performance on the pricing mechanisms is solid and satisfying the real market economics.

According to the Access to Medicines Index report in 2014, the affordability of medicines differs according to the payer whether patient or other reimbursement organization. The report assessed the pricing strategies considered by companies. It ensured that for multinational companies designing their launch of medicines, they consider socioeconomic factors for certain country in addition to the World Bank classification of country national income, i.e.: GDP. Moreover, the disease burden of

the country is another determinant for company strategy for need-based pricing according to a set of priority countries<sup>10</sup>.

As Egypt was one of the countries classified by the World Bank as LMIC, it was included in the report of the top 20 pharmaceutical companies. The report included companies that have brand medicines in addition to subset of generic medicines marketed in different countries. Access to medicines measured the company behavior in setting equitable pricing strategies and letting entry to the most affected markets with highest burden of the disease in scope. Equitable pricing strategies provided by the company is not the only indicator measured, but also the readiness for filing registration in the country to allow for access.

One other indicator included in the index measure of the top 20 pharmaceutical companies is the patenting practices. The more flexible strategies the company has to allow for equitable access and competition among their existing brand and generics in the country, the higher their performance in the index. Companies can publicly agree to waive their patent rights and their data-exclusivity in certain regions with poor population in order to allow for more competition and hence increase access to more affordable medicines. Companies are measured for their fair use of flexibilities in the Doha Declaration and Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement if they are recorded as engaging in lobbying activities pushing the access to affordable medicines backwards. The indicators measured under this pillar are disclosure of licensing practice, and patent disclosure, and endorsement of trade policy (TRIPS) flexibilities. The company should have "voluntary licensing"<sup>11</sup> strategies and "non-assert declarations"<sup>12</sup> for the patented products as well as technology transfer for medicines in scope.

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<sup>10</sup> Priority countries: are countries according to the index that have the most five countries having the highest burden of the defined-disease and classified as low-income countries by the World Bank.

<sup>11</sup> A contract through which the patent-holder (the licensor) voluntarily permits a contracting party (the licensee) for the manufacture and distribution of a product. A non-exclusive voluntary license is when the license can be agreed with multiple licensees.

<sup>12</sup> A legally binding commitment that contains an explicit set of conditions, including permitted actions and designated territories, for which the patent owner commits not to enforce patent rights. This allows for a generic version of a patent protected product to be produced.

It is of great value to relate the access and availability of NCD medicines to the IP issues and measure required by governments. Wanis (2009) mentioned that IP issue is one determinant in access to medicines along other underlying economic conditions, illiteracy and prescription and consumption patterns.

However, Mackey et al (2012) tested for any association between the NCD medicines on the Essential Medicines List (EML) and IP. Their results showed that none of WHO essential medicines has patent or data exclusivity. This important study exclude the patent issues from any concern of access to NCD and essential medicines. Any constraints of access to NCD essential medicines would be related to issues other than IP (Mackey, 2012).

As we referred earlier in this review of literature that different quality of brand and its generics may be recorded, however as long as Mackey et al (2012) revealed that no medicine on EML has patent or data exclusivity and, hence, manufacturing data and techniques for those NCD medicine on EML brand medicines are available for its generics manufacturers and no longer protected.

Non-Communicable Diseases (NCDs) affect adults in their productive years, require long term treatment and often cause disability. They can have more severe economic consequences for the individual and his or her family,—including decrease or loss of household income, impoverishment, loss of savings and assets, and reduced opportunities—than other illnesses. Amongst people suffering from chronic diseases in Egypt, for example, the probability of being employed is 25 % lower than the average, and their working time is reduced by 22 hours per week on average. NCD-related health care costs can also significantly affect the financial security of the households. (Rocco et al, 2011)

Acosta et al (2014) recommended that further research is required to evaluate the impact of the pricing policy on the medicines use and purchasing pattern. That is in our paper, we target the study of pattern of access to different medicine types in different socioeconomic areas.

Coming to the gap that this piece of research may cover in the literature above, this thesis adds to the literature by studying the association between the socioeconomic determinant represented by the rural and urban areas with contrast socioeconomic characteristics and the supply of medicine types; both brand and its generics. Supply side of brand versus generics with varying prices was not studied before for urban and rural areas. In some studies, only consumption pattern of generics was related to the patient characteristics of employment, literacy and education, age group.

## Chapter 3: Methodology

### i. Data source

In this research, we used secondary data published for the survey on medicines affordability and availability in Egypt conducted in 2013 (HAI, 2014). The data comprised 63 medicines treating Non-Communicable Diseases (NCDs).

Data collected from a field survey from pharmacy outlets measuring the affordability of NCD medicines. Selected list of medicines covering major NCDs in Egypt were surveyed for the brand product and price of their available generic equivalent. Medicines for study in 2013 were chosen from the national Essential Medicines List (EML<sup>13</sup>) in Egypt.

Brand pharmaceutical product belongs to the innovator company that got the first license and developed the molecule of the medicine. Generic pharmaceutical products are those products having the same molecule of the innovator and are manufactured locally by Egyptian companies or imported from company other than the innovator.

For the list of 63 medicines surveyed, prices of both brand and generic medicine type were recorded and calculated in different geographic areas covering seven governorates. Cairo, Giza, Qalyobia, Alexandria, Ismailia, Dakahleya, and Assiut were selected. Five pharmacy outlets were surveyed per area. A sum of 50 pharmacy outlets was surveyed and prices were recorded for the available brand medicine and one of its lowest available generic equivalent.

### ii. Study Design

The study has a cross-sectional design. Three-step inclusion conditions were made. The available medicines in all outlets were recorded in a snapshot from every outlet when the data was collected.

The three-step conditions were:

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<sup>13</sup> Essential Medicines List: is the list of medicines each country should have prime measures to secure access and market availability. The list pertain to country prevalence disease rate and priority health conditions.



1- Both brand and generic medicines are registered in MOH and marketed in Egypt. Any medicine with neither registered generics nor brand product in Egypt was excluded. If generic pharmaceutical products are marketed but the brand product is not registered, or if the pharmaceutical brand is registered and it has no generics registered, it is useless to include either in the study.

In other words, choice between a brand and a generic medicine types should be valid.

- 2- The medicine is on Essential Medicines List (EML).
- 3- Either medicines; brand and generic, was recorded in at least all areas; rural and urban. If one medicine with its two types (brand and generic) was not observed in at least one survey area, it was excluded.

The number of medicines we selected for our study is 39 medicines. Every medicine has one brand and product and one generic product; that is 78 product included in our study. These 78 medicines were recorded in 50 pharmacy outlets, that is our total observations are 3900 observations ( $n=3900$ ). Every observation was made when a medicine type whether brand or generic is seen in a pharmacy outlet.

Using this large number of observation is very healthy to the analysis of our paper. Data sets are used here to study the relationship between the supply of either generic or brand medicine to the different urban and rural areas from which data was collected.

From a social equity perspective, we set the null hypothesis that brand and generic medicines have equal availability in rural and urban settings.

**Table 7: List of medicines selected and their therapeutic classes (ATC classification) used in analysis**

	Medicine	Therapeutic Class		Medicine	Therapeutic Class
1	Acetyl salicyclic acid	Antithrombotic Agents	21	Lactulose syrup	Anti-constipation
2	Allopurinol	Anti-gout	22	Levodopa+Carbidopa	Anti-Parkinson
3	Amlodipine	Cardiovascular	23	Levothyroxine	Thyroid therapy
4	Atenolol	Cardiovascular	24	Lisinopril	Cardiovascular
5	Atorvastatin	Anti-hyperlipidemic	25	Loratadine	Antihistaminic
6	Betamethasone valerate	Corticosteroids	26	Losartan	Cardiovascular
7	Captopril	Cardiovascular	27	Meloxicam	Anti-Rheumatic
8	Carbamazepine	Anti-epileptic agent	28	Metformin 500	Anti-diabetic
9	Carvedilol	Cardiovascular	29	Omeprazole	Gastrointestinal
10	Clopidogrel	Cardiovascular	30	Paracetamol	Analgesics
11	Clozapine	Psycholeptic	31	Phenytoin	Antiepileptic
12	Diclofenac	Anti-Rheumatic	32	Propranolol	Cardiovascular
13	Digoxin	Cardiovascular	33	Ranitidine	Gastrointestinal
14	Epoetin alpha injection	Renal Failure/Antianaemic	34	Risperidone	Psycholeptic
15	Fluoxetine	Psychoanaleptic	35	Salbutamol inhaler	Chronic Respiratory
16	Furosemide	Cardiovascular	36	Simvastatin	Anti-hyperlipidemic
17	Glibenclamide	Anti-diabetic	37	Sodium valproate syrup	Antiepileptic
18	Gliclazide	Anti-diabetic	38	Soluble regular human insulin	Anti-diabetic
19	Ibuprofen	Anti-Rheumatic	39	Timolol eye drops	Anti-Glaucoma
20	Isophane human insulin	Anti-diabetic			

Relationship between the availability, recorded for both brand and generic medicine, and the type of socioeconomic class of geographic area; either urban or rural, will be analyzed by running Regression analysis.

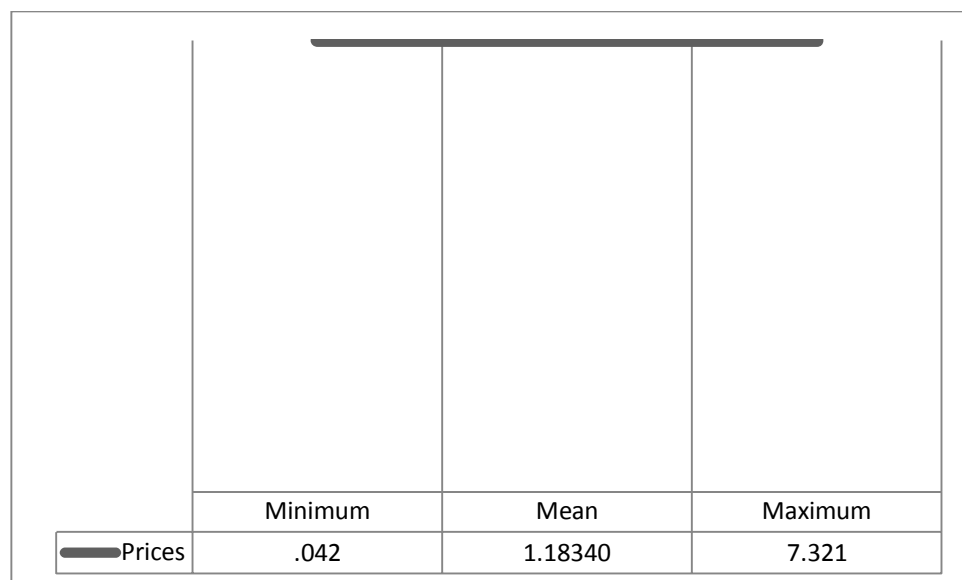
### iii. Organization of data

The list of 39 medicines with 78 brand and generic types in 50 pharmacy outlets was modeled. We organized the data for every medicine recorded and coded per observation. Each medicine type (brand/generic) was recorded 50 times once in every outlet yielding 1950 observation for all brand medicines and 1950 for all generic medicines. We had 3900 observations (n=3900).

As elaborated above that every medicine has one brand product and one generic equivalent. The observations were organized and responses were indicating the binary data for brand and generic medicine as 1 and 0, respectively.

Price used is the market price divided by the pack size (tablets, capsules, milliliters of solutions or syrups, doses of inhalations, grams of topical preparations, etc...) to standardize the price measured per medicine in cases when brand and generic medicines of the same API have different pack sizes; e.g.: pack of 120 ml with pack of 125, or pack of 20 tablets with pack of 30 tablets. These data was shown under "unit price" column.

**Figure 11: Descriptive of price variable included in analysis using SPSS software**



	Minimum	Mean	Maximum
Prices	.042	1.18340	7.321

### iv. Processing of data

In this model, dependent variable is brand/generic variable (br) coded as 1 for brand and 0 for generic.

Independent variables are: unit price variable (pr) recorded as observed, urban/rural (ur) coded as 1 for urban and 0 for rural. The number of observations were 3900 (n=3900).

Extreme values of price that are more than 10-folds of the mean price were excluded (34 observations) leaving final observations of n=3866. There were no missing cases.

#### **v. Limitations**

- 1- The study is a cross sectional data that shows only a snapshot of the availability of both brand and generic medicines selected for the survey. Further supply of the medicine in question may have been ordered prior to the survey and available at any other consecutive time.
- 2- While the number of observations are quite good(n=3900), the number of medicines used in this analysis is relatively low (78 medicines against over 14,000 medicine registered), and the number of outlets in the study (n=50) relative to the total number of pharmacies nation-wide is low (70,000)
- 3- Prices used are for the unit price in local currency (EGP). Further devaluation of the currency occurred but was not considered in this study.
- 4- The prices used were at that time of the survey in 2013. Some medicines may have increased/decreased in price due to some circumstances like shortages, or company appeals.
- 5- The prevalence rate for the diseases treated by the medicines covered in this study is not available at the national level. This is one of the important recommendations to point out in the end of this research to establish an Egyptian registry for each of the NCDs, and other diseases.

#### **vi. Statistical Tools**

In this research, we used Logistic Regression Analysis to assess the association between the socioeconomic characteristic of the areas and the probability of a brand or generic medicine is available.

In the Logistic regression, the dependent variable is a dummy variable (binary) either brand (1) or generic (0). The independent variables are also binomial rural as reference (0) and urban (1).

We used R programming software available online<sup>14</sup>. Codes for regression and diagnostics are included in this paper in the Annex. All factors described were not included in the final model. *P*-value and odds ratios were derived from this model. We also used the Statistical Package for Social Sciences software (SPSS).

**vii. Data Analysis:**

We used the Logistic Regression with following parameters considered:

(*br*) : is dependent variable Brand

(*ur*) : is independent variable Urban

(*pr*) : is independent variable Price

(*ur.pr*) : is interaction variable between the two independent variables Urban\*Price.

The Logit model :

$$\ln\left(\frac{br}{1-br}\right) = \beta_0 + \beta_1ur + \beta_2pr + \beta_3ur.pr + \mu$$

Where:

$\beta_0$  is the constant of the equation

$\beta_1$  is the coefficient for the urban/rural variable

$\beta_2$  is the coefficient for the price variable

$\beta_3$  is the coefficient for the interaction of urban and price variables

$\mu$  is the error term

$$br = \frac{1}{1 + e^{-(\beta_0 + \beta_1ur + \beta_2pr + \beta_3ur.pr)}}$$

It is easy to say that

$$\beta_0 + \beta_1ur + \beta_2pr + \beta_3ur.pr \rightarrow +\infty \quad \text{when } br \rightarrow 1$$

and when

$$\beta_0 + \beta_1ur + \beta_2pr + \beta_3ur.pr \rightarrow -\infty \quad \text{when } br \rightarrow 0$$

Then, *br* cannot be outside the range [0,1]

The estimated marginal effect is given as follows:

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<sup>14</sup> Programming language and software environment used for statistical computing and graphics. The R language is widely used among statisticians and data miners for data analysis.

$$\frac{\Delta br}{\Delta ur} = \frac{\hat{\beta} e^{-(\beta_0 + \beta_1 ur + \beta_2 pr + \beta_3 ur.pr)}}{(1 + e^{-(\beta_0 + \beta_1 ur + \beta_2 pr + \beta_3 ur.pr)})^2}$$

$$= \hat{\beta} \widehat{br} (1 - \widehat{br})$$

The logistic regression for the variables  $ur$ ,  $pr$ ,  $ur.pr$  gives the highest significance to the  $pr$  variable and highest Wald test value. Other variables significance were all above 0.05 significance level.

Knowing that External Reference Price policy used sets the generic price lower than its brand by 30 and 35% as stated earlier in the pricing policy followed in Egypt, there is a very strong relationship between both variables; brand and price. This strong relationship with the highest significance minimized the significance of the other variable and the interaction, in other words covered for any existing relation between the brand and urban variables.

To confirm what we had in the first estimate of regression, we estimated the regression again without the ( $ur$ ) variable and found that significance of the price ( $pr$ ) increased 10 times from 0.03 in the first model to 0.003 in the second one. That confirms the effect of significance of a highly significant variable in this equation to a relatively lower significant variable.

The association between medicine type (brand, generic) and the price is already established by the current policy of pricing.

To solve for that, we set *price* aside and estimate the model without the price variable to observe the significance of the other variable in absence of *price*.

The new equation would be as follow:

$$br = \beta_0 + \beta_1 ur + \beta_2 ur.pr ,$$

Where:

$\beta_0$  is the constant of the equation

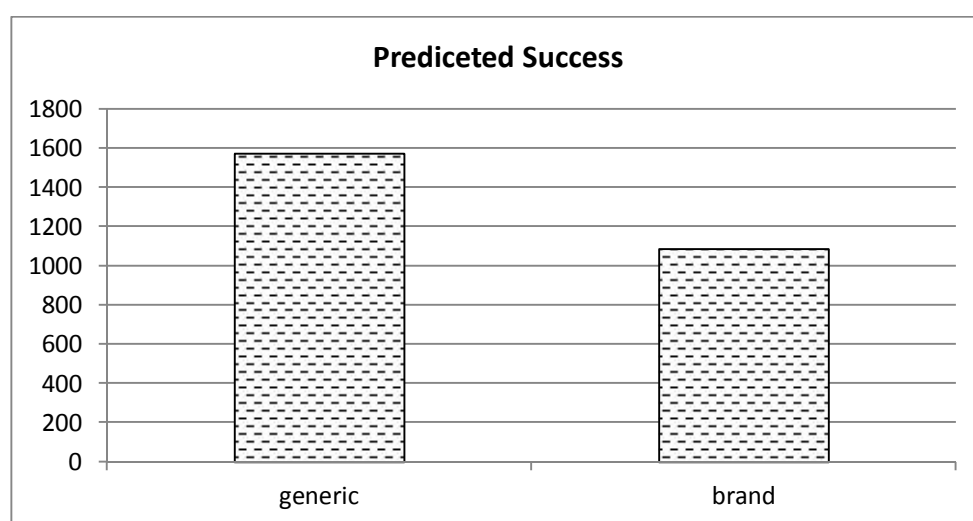
$\beta_1$  is the coefficient for the urban/rural variable

$\beta_2$  is the coefficient for the interaction urban of and price variables

The regression in this scenario was better than with the variable *pr* giving very high significance lower than the 0.05 significance level and Chi square value for the model was 204.69 with degrees of freedom equals to 7 shown in the Annex.

The model classification shows the success rate of 73.6 %. Where the percent of predicted cases to the actual observed cases are true (i.e.: that is the brand medicines were predicted and generic medicines were predicted with success rate of 73.6% shown in Figure 12: Predicted success for the regression model).

**Figure 12: Predicted success for the regression model**



The significance of the variables and their Wald values are shown below.

Where the final equation can be put as follow:

$$br = 0.75 + 1.33ur + 1.38ur.pr$$

Sig.	.000***	.009**	.000***
Wald	47.77	6.915	131.634
n =	3866		

That is the null hypothesis is rejected and  $\beta_1$  is not equal to zero. That is the change in urban variable from rural (0) to urban (1) will increase the probability of brand medicines by 1.33 times than generic.

The *ur.pr* coefficient refers to that with reference to urban area fixed, when the price increases by one unit, the probability of the medicines to be a brand increases by 1.38 folds.

These interpretations confirms the alternative hypothesis that for urban areas there is a higher probability to have brand medicines available than generics, and in rural areas, the probability for brand medicines is lower. Given the area is fixed in urban, as the price of the medicine increases, the probability that it is a brand medicine is increased by 1.38 than in rural areas.

So reject the null hypothesis of equal availability of brand product in rural and urban.

### **Interpretation of results**

In this paper, we modeled the data for estimating the association between the probability of supply of brand or generic pharmaceutical product in urban and rural areas representing the different socioeconomic areas in Egypt.

A total of 39 different medicines distributed in 16 therapeutic groups (ATC- level1) were identified.

In our model, we organized the data and estimated the regression for the 3900 observations in which all medicines (brand and generics) were recorded in all 50 pharmacy outlets. Dependent variable which is the supply of brand/generic was dummy variable 1, and 0 for brand, generic type of medicines, respectively.

Prices were used as independent continuous variable. Extreme values for the unit prices were excluded. The maximum price was 7.32, minimum was 0.042, and the mean was 1.18.

The regression of supply of either brand or generic is strongly related with price rather than for urban and rural nature of the outlet. The association between medicine type (brand, and generic) and the price is well established and known. This association is not the focus of our study here. The significance of the other dummy variable (urban=1 and rural=0) and the interaction (urban.price) used were minimal. This minimal significance was attributed to the strong significance of the price variable included. So, regression was estimated again dropping the price variable. The model gave 73.6 % success rate of the predictions.

The significance for the two variable; urban and urban.price variables were high at 0.009, and 0.000; respectively. The coefficient logs produced were -0.288 for the



constant, 0.288 for the urban, and 0.326 for the urban.price, and odds ratio were obtained as 0.75, 1.334, 1.386; respectively.

It is clear now from the final equation set for the model:

$$br = 0.75 + 1.33ur + 1.38ur.pr$$

that, given the socioeconomic characteristic of the area in which pharmacy outlet is located, the probability for brand medicine to be supplied is 1.3 times higher for urban rather than the area was rural. While in urban setting, and with the increase in price, the probability of the medicine supplied is brand increases by 1.38 times than rural areas. Rural areas are more likely to be supplied with generics rather than urban. The alternative hypothesis is now true. Brand medicines are more likely to be supplied and available in urban areas. Urban areas are with higher socioeconomic level than rural areas in Egypt. In this analysis, we did not include detailed characteristics of the urban and rural socioeconomic status as income, education level, and employment-unemployment as data is not available and left for future studies. These detailed characteristics are related to consumers not to the supplier and their consumption patterns. The socioeconomic class of the area as a whole whether urban or rural is considered for the supply of either high priced brand or low priced generic.

The results representation in our analysis is around 43% of Egypt population (CAPMAS, 2016), the seven governorates included had census of around 38.6 million people.

**Table 8: Governorates population included in the study**

Governorate	Population (census in million)	Socioeconomic class
Alexandria	4.805	Urban
Assuit	4.241	Rural
Cairo	9.265	Urban
Dakahleya	5.942	Rural
Giza	7.575	Mixed
Ismailia	1.77	Urban
Qalyoubia	5.098	Rural
<b>Total Governorate Populations</b>	38.696	43% Percentage of total population
<b>Total Egypt</b>	90.8	

## Chapter 4: Discussions and recommendations

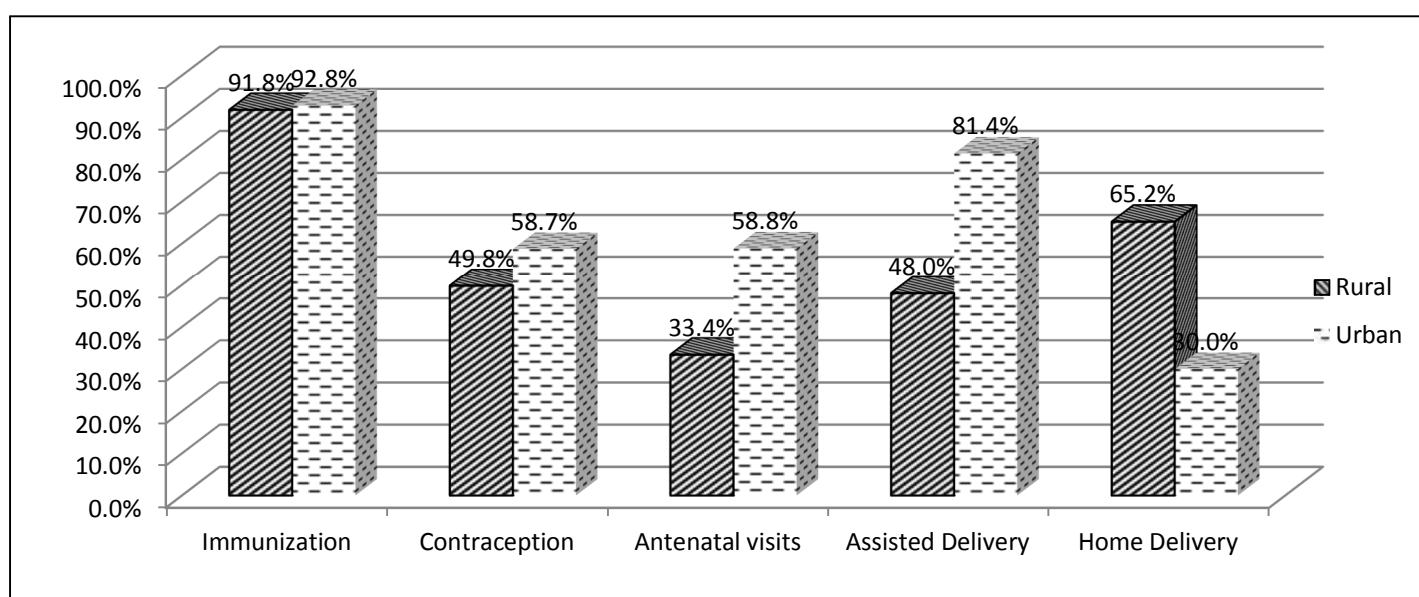
### Insurance coverage

While only 58% of Egyptians are covered by the public health insurance system, the financial burden of any illness is enormous as the percentage of the uninsured is higher in rural residents and those in the lowest socioeconomic levels (USAID, 2010).

In Egypt, although there is a relatively well-established medical insurance system providing medical services through a large number of public facilities; it does not cover the whole population. In order to be under the umbrella of the state medical insurance system, one has to be either a school student or a government employee. Accordingly, the high school dropout rate coupled with the high unemployment rate in the formal economy; mainly in the low-income level households have led to a high percentage of underprivileged patients who are uninsured. These patients pay out of their pockets when in need for any medical intervention, let alone medicines and operations. These out of pocket expenses represent a real burden.

The access to health care services assessed in rural and urban areas in Egypt resulted in higher access to basic health care services in urban areas with higher socioeconomic pattern (Boutayeb, 2011). For example the access to assisted delivery for women in 2011 was around 81% and 48% for urban and rural Egypt; respectively.

**Figure 13: Rural-urban access to health services in Egypt.**



(Boutayeb, 2011)

### **Expenditure on health**

Total health expenditures constitute 5.6% of GDP, and while private health expenditure is 60% of the total health expenditure, 97.6% of private health expenditure is for out of pocket (OOP) expenditure. Pharmaceutical expenses comprise 34.2 percent of total health expenditure and 42.6 percent of OOP spending on healthcare (WHO and WB, 2014).

The public supply chain in MOH is vulnerable and is not properly structured leaving public health facilities with frequent stock-outs. As a result, patients often do not obtain their medication at the healthcare facility where it is prescribed, 90% of patients reported buying medication at a pharmacy, but only 10 % obtained medication at the facility itself (World Bank, 2010). Coupled with the absence of prescribing regulations, the dispensing of available medicines that are not actually needed by patients in public health care facilities is resulting in medicine misuse and misconsumption data. This has caused entry into the market of low-quality generics.

### **Access to Medicines**

A socially equitable system provides the same level of quality health services to people with the same need, regardless of socioeconomic status, gender, place of residence, or any other potential difference, while an accountable system demonstrates and takes responsibility for performance to create high-quality health care (WB, 2015). Egypt scored 32.1 in 2004 on Gini<sup>15</sup> Index and 30.1 in 1995 while in 2008 its score was 30.8 (WB, 2016). Egypt has permanent inequality around the same range with no powerful intervention since 1995 introduced to alleviate this inequality. There are 17 pharmacists per 10,000 of the population. The number of private pharmacy outlets in Egypt is around 8 pharmacies per 10,000 of the population (MOH, 2015). By calculating the number of people entitled to benefit from the pharmacy outlet, every 1250 citizens are benefiting from every outlet assuming even distribution of outlets all of equal size businesses. In reality, this is not the case because there is heavy distribution of pharmacies in urban than rural.

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<sup>15</sup> Gini index measures the extent to which the distribution of income; consumption; expenditure among households within an economy that deviates from a perfectly equal distribution. Considered as a measure for social equity, Gini index of 0 represents perfect equality, while an index of 100 implies perfect inequality.

Access is measured primarily by the availability of affordable medicines (WHO, 2016). Affordability and prices survey was conducted in 2013 and found that mostly all medicines on the EML List for chronic diseases are affordable (HAI, 2014). As affordability was measured per medicine type (brand, and generic), availability here was measured per medicine type per geographic area having different socioeconomic characteristics.

In urban and rural areas, poverty levels and hence expenditure on health is greatly different. In rural areas with lower socioeconomic level, however, the spending on health as percentage of annual individual expenditure is higher than urban areas. With the low economic and social pattern, illiteracy, and weak health awareness, disease burden is high in rural areas rather than urban. This can be illustrated while rural areas have more access and availability pattern of generic lower priced medicines, they, moreover, spend more OOP for their treatments. Chronic illnesses are life-long conditions that need permanent supply of medicines to improve health status and come in the good labor force for the society.

The increased OOP expenditure on health is not only due to uninsured patients but also due to the medicines shortages in public healthcare system for those who are publicly insured. The public pharmaceutical supply chain is vulnerable and not well-organized leaving weakness points of shortages and limited budgets and irregular supply to served areas.

### **Globalization and access to medicines**

The impact of globalization on the pharmaceutical market is elaborated in cases of medicines with patents. In Egypt, law number 82/2002 has several articles which ensures protection of public health preventing the abuse of the exclusive data protection allowing for voluntary licensing by the innovator and compulsory license by the government in cases of epidemics and public health crisis. Such actions are called TRIPS flexibilities which resulted from the Doha declaration

To overcome this restriction and to protect the public health, several measures had been proposed by Doha Declaration; for example, compulsory licensing, voluntary licensing (breaking patency voluntarily and locally manufacture the medicine), importation from a country where patent is not valid, paying the patent company a reasonable fee to allow for generics, or parallel trade.

Parallel trade is where a patented medicine price in a country is lower than its price in another country. The medicine is transferred from the lower priced to higher priced country. Although this can be a solution to increase access to patented medicines, parallel trade can potentially benefit traders and mediators rather than patients themselves. This also creates parallel markets that can undermine the efforts for equitable international pricing system. The innovator company may be reluctant in the future to run the medicines in LMIC due to probabilities of parallel trade.

### **Egyptian medicines regulatory intervention**

While local pharmaceutical market in Egypt has the characteristics of the market economy, the government intervention took different directions. CAPA, under the Ministry of Health, is the main regulatory body of the market and such interventions mostly initiated there.

**The first intervention in market is the "box" policy for registration.** This policy created a restricted competition whereas monopoly at certain cases. The policy had mainly been proposed for introducing medicines to the market covering all therapeutic indications specifically those that are not of interest; e.g.: orphan drug, and low-profit margin products, medicines treating less prevalent and neglected diseases. While this policy is undesirable in Egypt limiting the competition, it was recommended to United States Food and Drug Administration (FDA) to restrict the entry of suppliers to remain in the interest of supplying medicines (Brown, 2016)

To acquire its required impact, the "box" policy should be allowed for medicines with narrow therapeutic index with rigorous measures that ensure the equivalent quality and characteristics of both brand medicine and its generics.

Quality of both brand and its generic medicine should be monitored closely not only by the bioequivalent tests but also by some other test to ensure the in-vivo availability and onset of action leading to the same desirable therapeutic effect.

**The second intervention is the obligatory/compulsory pricing;** an intervention made by most government to ensure affordability to patients and prevent any monopolistic behavior on the one hand, and to limit health care expenditure on the other hand.

External reference pricing used in combination with mark-up regulation kept prices as low as possible. Industry and pharmacists were satisfied with the existing prices for

definite time span till the devaluation of Egyptian pound took place. Pricing of medicine before devaluation differs than after, e.g.: a medicine priced in one reference country at \$5 value will have local price of EGP 34 in 2013 while in 2016, it will be priced at EGP 39.5. Difference is around 14 % in the exchange rate, while global market prices are held stable. Noting that prices are approved for the life of Marketing Authorization (MA) period of 10 years and usually price revision will not occur upon re-registration process.

On the flip side of the picture, the industry players including distributors and scientific offices study market well and define their registration, production, and importation plans based on their profitability rather than protecting public health.

### **Market Dynamics**

We will apply the understating to this issue in the inputs of the market economics related to the pharmaceutical market as follows in this section.

Medicines are inelastic in demand; increase in prices will not impact the quantity purchased. Inelasticity of medicines for chronic conditions and life-saving situations is relatively higher than those used for acute conditions (WHO, 2015). As medicines used to protect health, the value of medicine is high to the patient paying to keep their health intact as much as they could and its high value differs from patient to patient according to the outcome it achieves. Medicines cannot be freely re-traded or resold by patients.

The pharmaceutical market is not a perfect competitive market in which variety of reasons allow for market asymmetry. The asymmetry resulted from the lack of information on the demand side. Patients do not have the proper knowledge of their method of diagnosis or protocol of treatment as they refer to physicians to take decisions on behalf of them. Patients are left at the physicians' discretion, and sometimes at the pharmacist's directions during dispensing or consultation.

From the supplier side, there is some bias to suppliers in which the pharmaceutical companies can influence the physicians' decision for treatments. Research and development that company had done in the clinical and preclinical phases are not always published and still exclusive for the patency time. Physicians are prescribing medicines based on the available knowledge, so companies can influence the physicians' tendency to prescribe one medicine or another.

In Egypt, there are no clear prescribing guidelines. There is no clear guidance or regulations regarding the promotion of prescription medicines for pharmaceutical suppliers. The role of the pharmacist as drug expert is not practiced on the ground. The legislative structure has to be reformed. The only limitation to bias in information knowledge is the regulation restricting the sale of medicines only by pharmacists. While the demand side is as much important as the supply side, the irrational use of medicines adds to the cost of health care interventions by the medicines misused qualitatively and quantitatively. Lack of rational use of medicines prevents the right decisions regarding both demand side in determining proper procurement decisions and the supply side from proper supply and manufacture decisions made in the pharmaceutical market.

If we consider public health is public goods, the government should have the capabilities to regulate and protect the public health. This occurs by the regulating pharmaceuticals and establishing control on the market preventing the falsified medicines or counterfeit to be on the market. Controlling market can take other forms of putting some barriers to entry of any medicine that can harm the public health instead of saving it. So the regulations of pharmaceuticals and pricing policy are part of government intervention to protect the public health as public goods. Subsidies should be provided to pharmaceutical suppliers to ensure the appropriate supply to the market to sustain the protection of public health, and prevent any shortage in medicines.

Pricing can also be controlled by market power of the demand side. Some times to influence markets, suppliers may lobby to form oligopoly that change the market price of certain medicine category alternatives. The intervention of the government in this case would be best if monopsony is practiced. Monopsony is the case when there is only one consumer on the demand side, while there are multiple suppliers in the market. Every supplier will offer the best price for the medicine and the competition is for the sake of the patient. One form of the monopsony is the public/social health insurance scheme that covers all population.

Monopsony also can be exerted in cases of patented medicines when there is monopolistic power from the supplier. The demand power by single player on the demand side will decrease the supplier power allowing for negotiating price. This can

also take place when one or two medicines are registered for one API. If the API is used to treat certain chronic condition and the medicines are imported, then the monopolistic power of the supplier can be expected. In this case prevalence<sup>16</sup> rates and disease pattern are extremely important to the monopsony of the government and to induce generic competition because leaving the medicines supply used for the chronic condition or NCD under the supplier's power is failure to protect the public health. Pooling of demand of medicines, not only within the health care system, but also in the wider society, is needed to increase purchasing power and insure accessibility.

One of the pricing policies adapts the maximum price, which is a price ceiling and the medicine in the market should not exceed that price. Price ceiling will not be effective if it is above the equilibrium price, however it may generate shortages if it is far below the equilibrium. We can recommend here that price ceiling can be followed provided that the equilibrium price should be known to the regulator.

Price controls will be optimum if price ceilings made are satisfying the market equilibrium or very closely around it (equilibrium here means demand of medicines; i.e.: prevalence of diseases and standard treatment guidelines, are met with proper supply type and quantity).

For the medicines demand to be accurate and powerful, the single buyer concept (social health insurance covering majority of population) shall potentiate the power of the regulator to set prices. Prices to be fair meeting the supplier's expectations and planning, the exact demand for medicines should be based on the consumption pattern for every medicine and to be related to the prevalence rate of diseases.

The consumption pattern for medicines can be easily obtained by a new intervention some governments began to use recently called "Pharmaceutical Track and Trace" system and policy. In the policy, every medicine registered in the country is traced per pack. Every pack of the medicine is recorded on the central database once it is manufactured and labeled a unique code for identification. Any transaction on this specific pack will be recorded by the database allowing for exact map of distribution and patterns of consumption and locking the market against any parallel

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<sup>16</sup> The prevalence rate of diseases is the proportion of population who has a particular disease over a specified period of time. This proportion includes not only new cases, but also old cases remained ill during the specified period in time.



illegal trade of falsified counterfeit medicines provided that all stakeholders are involved in the process. Upon analyzing the data we have for every medicine, then national demand is well known and the government can leverage to set the ceiling price at the equilibrium price. In this scene, both sides of suppliers and buyers are recorded and any surplus would be apparent.

Coupled with the fair health insurance scheme, the "Pharmaceutical Track and Trace" can effectively integrate with the reimbursement organizations and monopsony will be exerted in a perfect scenario. Brand and generic pharmaceutical products will be the same in determining the fair market equilibrium price and lower/higher socioeconomic class do not have to worry about their healthcare cost or access to either type of their medicine (brand, and generic). Pricing policy in this case may follow either "Price Ceiling" or "Volume Agreement" policy. The first can be applied when insurance coverage is not covering the whole population and still there are proportions of population have to pay OOP expenses to buy their medicines.

The second policy, "Volume Agreement", is best fit when there is single buyer with exact demand quantity when the negotiating power will be high. Using pharmacoeconomic evaluations to help with setting the fair market equilibrium price is recommended. Under "Volume Agreement", the agreed drug price is based on a forecast volume of sales. If the actual volume exceeds the forecast, the drug price usually has to be lowered. The health insurance coverage has a prominent advantage of lowering pricing by the power of purchasing and reimbursement through the government, or health insurance body. This recommendation is feasible upon coverage of majority of the population by health insurance scheme.

Governments' interventions should maximize the buying power by pooling of purchases. The government should be armed with some essential tools, for example resources for pharmaco-economic analysis, informed decisions about the buying and selling parties in the market, the segmentation using International Drug Price Indicator Guide (MSH, 2016). The utmost goal to protect the public health will be done in a perfect behavior.

Most of the evidence from LMIC suggests that health insurance is associated with 1- increased use of medicines, 2- a reduction in the financial barriers to access, 3- more rational use, 4- and improved health outcomes (Faden et al, 2011).

The social health insurance should use internal generic reference pricing to set reimbursement rates. This recommendation has combined effects. Although this can successfully reduce medicine prices and encourage patients to choose more cost-effective medicines, generic reference pricing may not reduce overall medicine expenditures since it does not guarantee efficient medicines prices or impact the quantity of medicines prescribed (Faden et al, 2011).

Focusing on individual strategy for medicines improvement will produce non-preferable outcome. Combined strategies have to be pluralized and put in place to integrate one another. For example, in Kyrgyzstan a combination of generic reference pricing, consumer education about payment responsibilities, and price negotiation with suppliers established stable market pricing for medicines and improved patient access (Faden et al, 2011).

Egypt should use leverage to improve supplier and consumer practices, and to potentially lower industry prices, insurance systems with substantial membership can have overall effects on the health sector itself as externalities to combined medicines strategy. Consolidated system of public purchasing of medicines should be in place allowing for lower transaction costs and increased leverage for negotiating prices with the suppliers.

While the burden of NCDs is rising, it can constitute a major health challenge of access to affordable NCDs medicines. The government can use differential co-payment level for insuring consumers. This will act as an incentive for patients to choose the medicine of interest according to their preferences not according to the supplier. Moreover, neglected and orphan diseases common in the lower socioeconomic class should be resolved properly through Social Health Insurance.

The results of innovative research into needed medicines should be regarded as a global public good. Under the present system of incentives based on exclusive property rights, public and private investment in R&D is recovered through a temporary monopoly that results in high non-competitive prices. Unless alternative mechanisms are established that isolate incentives for innovation from prices, regulators should be aware that pricing can be regarded as a reward for past innovation and incentives for future R&D.

The argument of choice between brand and generic is assuming that quality is guaranteed. National regulatory authorities for medicines in countries have the prime responsibility to ensure that medicines in use are safe and of assured quality, preventing the presence of falsified or substandard medicines in the market.

Poor-quality medicines are known to cause harm to patients, not only suboptimal treatment outcomes but also serious disability or death in some cases. Regulatory authorities for medicines in low- and middle-income countries often have inadequate capacity to properly monitor the quality of medical products along their entire life cycle, including oversight of pharmaceutical company activities to ensure compliance with good manufacturing practices and other standards that ensure that both locally manufactured and imported medicines are of adequate quality and efficacy (WHO, 2015). Quality should be regularly monitored and ensured against global standards for both medicines; brand and its generic. Good governance for medicines framework to enhance the regulatory performance should be followed.

Solutions for the social equality with respect to availability of both brand and generic medicines in the urban and rural areas are required. On the one hand, social health insurance, illiteracy eradication, and increasing awareness of healthcare in rural areas may help increase availability of brand medicines in lower socioeconomic areas. On the other hand, improving availability of generics in urban areas may require assured equal quality of generic medicines, setting regulations for prescription medicines guidelines and prescribing medicines in non-proprietary names. The utmost goal to protect the public health will be done in a perfect behavior.

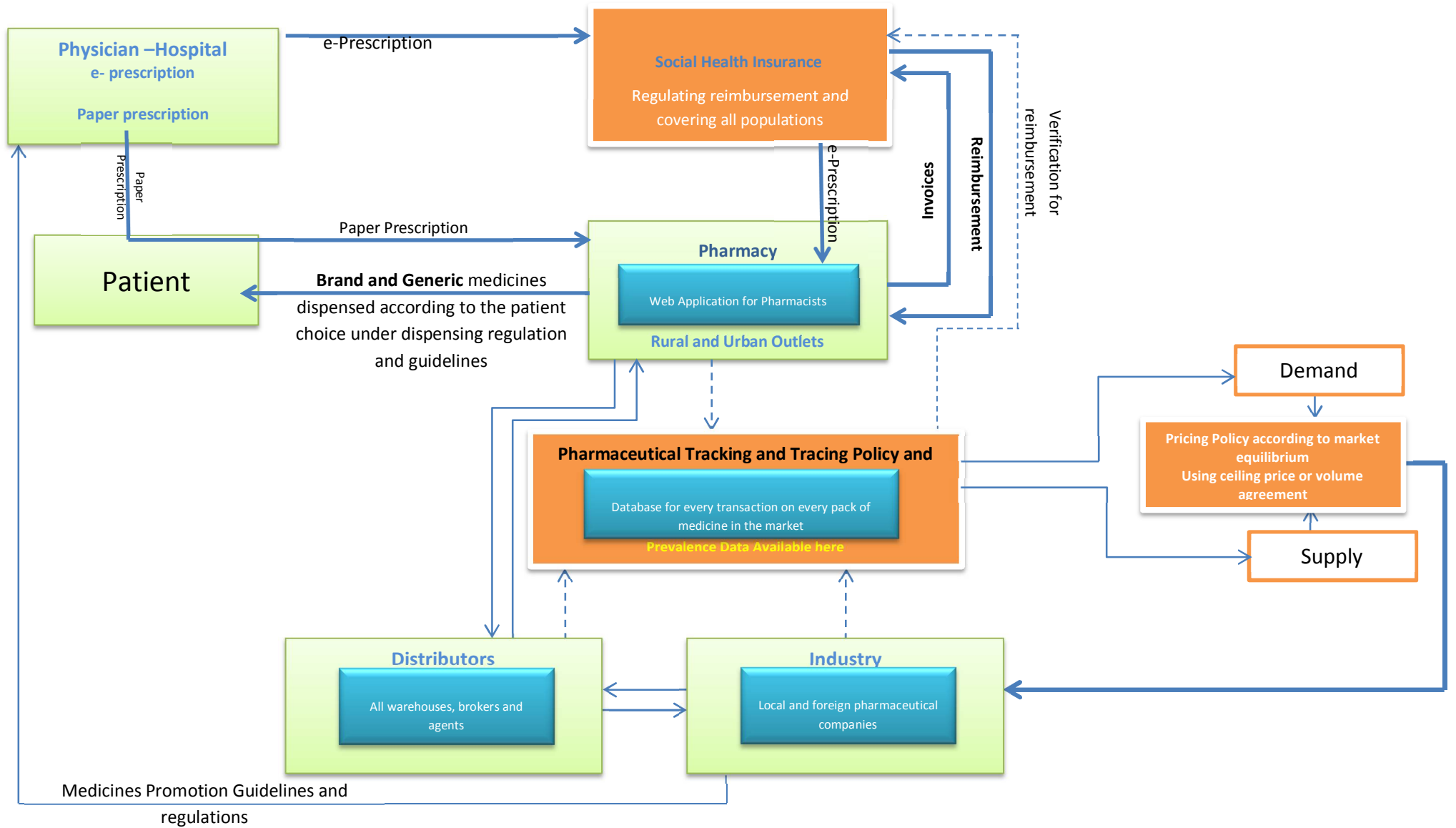
The good governance in medicines should allow for transparent practices in pricing. Conflicts of interest should be declared for all market stakeholders and regulators. The non-profit organizations and other society members should have role in the negotiating power of prices.

The good governance for medicine framework should be monitored and evaluated periodically with the assistance of WHO. Transparency measures should be in place.

The following Figure 14: Visual presentation of policy intervention and author's recommendations shows how the implementation of some recommendations can explicitly improve the overall performance of the healthcare system and

governance. Social health insurance coupled with "Track and Trace for Pharmaceuticals", patients can be dispensed their medicines of choice when prescribed by the physician. When the physician follows the prescribing guidelines, and when industry adheres to the medicines promotion regulation, patient choice of either medicine can be well practiced. Both generic and brand medicines will be available for the patient in either urban or rural areas. The "Pharmaceutical Track and Trace"; where all market transactions for all medicine packs, will be used to verify the reimbursement system, and to generate real-time data for supply and demand in the market allowing for equitable and fair pricing policies. Such policies and practices will lead to the equilibrium of the pharmaceutical market in Egypt.

Figure 14: Visual presentation of policy intervention and author's recommendations



## Conclusion

Medicines are important treatment interventions to promote health for people. Every medicine has a brand and generic product. Equal access to both types of medicines is part of equal access to health care in different socioeconomic areas. In this research, we used secondary data published for the survey on medicines affordability and availability in Egypt conducted in 2013 (HAI, 2014). We applied some inclusion criteria and 39 medicines were selected treating Non-Communicable Diseases (NCDs).

Our hypothesis stands for the assumption of social equity that presumes equal access to medicine alternatives for varying rural/urban population especially in chronic conditions that last long and necessitate treatments for life.

We modeled the data and used logistic regression. Results were produced using statistical software.

Primary findings show that rural and urban areas have different pattern of market supply; hence availability of both brand and generic medicine types. The urban areas are 1.3 times higher than rural to be supplied with brand type medicines. In the same settings of socioeconomic area, the probability of supply of brand rather than generic medicines increases by the increase in price.

Social health insurance coupled by pharmaceutical Track and Trace system and combined pricing mechanisms should be in place to insure equilibrium between market supply and demand and equal access to medicines. Guidelines for promotion of prescription medicines, guidelines for prescribing practices should be in place to improve the market equilibrium.

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**Annex I: Statistical results in SPSS**

Descriptive of the data variables used in logistic regression:

**Available**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Not Available	895	23.2	23.2	23.2
	Available	2971	76.8	76.8	100.0
	Total	3866	100.0	100.0	

**Urban/Rural variable**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Rural	1933	50.0	50.0	50.0
	Urban	1933	50.0	50.0	100.0
	Total	3866	100.0	100.0	

**Brand/Generic variable**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Generic	1933	50.0	50.0	50.0
	Brand	1933	50.0	59.0	100.0
	Total	3866	100.0	100.0	

**Price variable**

	Minimum	Maximum	Mean	Std. Deviation
pr Valid N (listwise)	.042	7.321	1.18340	1.503883

**The best fitting Model**

**Goodness of Fit**

Step	Chi-square	Df	Sig.
1	204.691	7	.000



**Classification Table<sup>a</sup>**

Observed			Predicted		
			<i>br</i>		Percentage Correct
			generic	brand	
Step 1	<i>br</i>	generic	1574	356	0.41
		brand	849	1087	0.28
Overall Percentage					<b>0.73</b>

a. The cut value is .500

**Parameter Estimates**

		Estimate	Std. Error	Wald	df	Sig.	OR
Location	Constant	-2.880E-01	.101	.000	1	.000	.750
	<i>ur</i>	.288	.110	6.915	1	.009	1.334
	interaction	.326	.028	131.634	1	.000	1.386

**Other Models**

- 1- The Regression of Brand (*br*) with both variable urban (*ur*), and price (*pr*) and interaction variable (*ur.pr*):

**Parameter Estimates**

		$\beta$	S.E.	Wald	df	Sig.	OR
Location	Constant	.130	.118	1.210	1	.271	1.138
	<i>ur</i>	-.158	.125	1.605	1	.205	.854
	<i>pr</i>	.216	.103	4.376	1	.036	1.241
	interaction	.110	.107	1.060	1	.303	1.117

- 2- The Regression of Brand (*br*) with variable price (*pr*) and interaction variable (*ur.pr*):

**Parameter Estimates**

		Estimate	Std. Error	Wald	df	Sig.	OR
Location	Constant	.271	.039	47.437	1	.000	1.311
	interaction	.040	.095	.180	1	.671	1.041
	<i>pr</i>	.279	.094	8.836	1	.003	1.322

## Annex II : Statistical Calculations in R

The statistics calculations done in R software were following the model iterations as follow:

The code used for programming of the data file as to do the following:

- 1- Read data file
- 2- Summary of data file
- 3- Programming of logistic regression parameters and variables
- 4- Testing for significance and other parameters evaluations.

```
# read data file, name it "m"
m<- read.csv("m.csv", TRUE)
# give summary about the data
summary(m)
#show part of data file
print(head(m))
#creating logistic regression "g" for data with dependent
variable is br and independent variable ur with interaction of
ur.pr excluding the pr variable
g<- glm(br~ur+(ur*pr)-pr, data=m, family="binomial")
# give summary of the regression parameters
summary(g)
# give the odds ratio for parameters
exp(coef(g))
```

The results are shown in R as follow:

```
  av br ur      pr
1  1  1  1  7.3214
2  1  1  1  7.3214
3  1  1  1  7.3214
4  1  1  1  7.3214
5  1  1  1  7.3214
6  1  1  1  7.3214

Call:
glm(formula = br ~ ur + (ur * pr) - pr, family = "binomial",
data = m)

Coefficients:
                Estimate              Pr(>|z|)
(Intercept)    -2.88e-1             0.000 ***
ur              -0.28813            0.009  **
ur:pr           0.32608             <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Number of Fisher Scoring iterations: 4
Odds ratio
(Intercept)          ur          ur:pr
0.750769            1.334243      1.386868
```

Showing results for the regression with the independent variable urban (ur), price (pr), and interaction variable urban\*price (ur.pr):

```
#creating logistic regression "g1" for data with dependent
```

```
variable br and independent variables ur, pr with interaction  
of ur.pr variable  
g1<- glm(br~ur*pr, data=m, family="binomial")  
# give summary of the regression parameters  
summary(g1)
```

The following results were produced:

```
Call:  
glm(formula = br ~ur * pr, family = "binomial", data = m)  
  
Coefficients:  
                Estimate                Pr(>|z|)  
(Intercept)      0.130460                0.271  
ur                -0.158262                0.205  
pr                0.216864                0.036 *  
ur:pr             0.110354                0.303  
---  
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Showing results for the regression with the independent variable price (pr), and interaction urban\*price (ur.pr) variable:

```
#creating logistic regression "g2" for data with dependent  
variable br and independent variables pr with interaction of  
ur.pr variable excluding the ur variable  
g2<- glm(br~pr+(ur*pr)-ur, data=m, family="binomial")  
# give summary of the regression parameters  
summary(g2)
```

The following results were produced:

```
Call:  
glm(formula = br~pr+(ur*pr)-ur, family = "binomial", data =  
m)  
  
Coefficients:  
                Estimate                Pr(>|z|)  
(Intercept)      0.271460                0.000 ***  
pr                0.279864                0.003 **  
ur:pr             0.040354                0.671  
---  
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

### Annex III: Egypt affordability survey findings

Some of the findings shown in the affordability survey for NCDs medicines conducted in Egypt in 2013 (HAI, 2014). The days of wage spent for medicines are based on minimum wage projected in 2014 to EGP1200 (EGP40/ day) .

Medicine and number of units required for 30-days treatment	Number of days of wage required to purchase the treatment for 30 days (B=Brand medicine, G=Generic Medicine)
<b>Diabetes</b>	
Glibenclamide 5mg x60	0.5 B / 0.2 G
Metformin 500mg x90	0.7 B / 0.5 G
Gliclazide 80mg x30	0.3 B / 0.2 G
Isophane insulin 100IU 10ml	0.8 B / 0.8 G
Regular insulin 100IU 10ml	0.8 B / 0.8 G
<b>Cardiovascular disease</b>	
Amlodipine 5mgx30	1.7 B / 0.6 G
Atenolol 50mgx30	0.4 B / 0.1 G
Captopril 25mgx60	0.8 B / 0.5 G
Carvedilol 25mg x30	2.1 B / 0.9 G
Digoxin 0.25mg x30	0.1 B / 0.1 G
Lisinopril 10mg x30	1.1 B / 0.6 G
Losartan 50mgx30	2.8 B / 1.4 G
Atorvastatin 10mg x30	3.2 B / 1.7 G
Simvastatin 20mg x30	4.3 B / 2.1 G
Acetyl salicylic acid 100mg x30	0.4 B / 0.1 G
Clopidogrel 75mg x30	5.5 B / 1.5 G
<b>Respiratory disease</b>	
Salbutamol 100mcg/dose x1 inhaler (200 doses)	0.3 B / 0.3 G
<b>Mental health /neuroleptic disorders</b>	
Fluoxetine 20mg x30	3.5 B / 0.7 G
Carbamazepine 200mg x90	1.2 B / 1.0 G
Clozapine 25mg x90	1.8 B / 1.2 G
Risperidone 2mgx90	14.0 B / 5.0 G
<b>Other NCDs</b>	
Diclofenac 25mg x60	0.6 B / 0.3 G
Ibuprofen 400mg x90	4.1 B / 3.2 G
Levodopa+carbidopa 250/25mg x90	4.5 B / 2.7 G
Omeprazole 20mg x30	2.9 B / 0.7 G

**Annex IV: The pricing sources in different countries**

<b>COUNTRY</b>	<b>TITLE</b>	<b>WEBSITE</b>
Australia	Schedule Pharmaceutical Benefits	<a href="http://www.pbs.gov.au/html/home">http://www.pbs.gov.au/html/home</a>
Austria	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Bahrain	Ministry of Health	<a href="http://www.moh.gov.bh/EN/E-ervices/DrugPrices.aspx">http://www.moh.gov.bh/EN/E-ervices/DrugPrices.aspx</a>
Belgium	Institut national d'assurance maladie-invalidité / Rijksinstituut voor ziekte- en invaliditeitsverzekering	<a href="http://www.inami.fgov.be/">http://www.inami.fgov.be/</a>
Brazil	Banco de Precos Em Saude	<a href="http://bpreco.saude.gov.br/bprefd/owa/consulta_inicio">http://bpreco.saude.gov.br/bprefd/owa/consulta_inicio</a>
Canada	Patented Medicine Prices Review Board (PMPRB)	<a href="http://www.pmprbcepm.gc.ca/english/view.asp?x=572">http://www.pmprbcepm.gc.ca/english/view.asp?x=572</a>
Canada	Ontario Drug Benefit Formulary / Comparative Drug Index	<a href="http://www.health.gov.on.ca/english/providers/program/drugs/odbf_mn.html">http://www.health.gov.on.ca/english/providers/program/drugs/odbf_mn.html</a>
Czech Republic	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Denmark	Medicin priser	<a href="http://www.medicinpriser.dk/">http://www.medicinpriser.dk/</a>
Finland	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
France	L'assurance maladie	<a href="http://www.codage.ext.cnams.fr/codif/bdm_it/index_presentation.php?p_site=">http://www.codage.ext.cnams.fr/codif/bdm_it/index_presentation.php?p_site=</a>
France	Ministry of Health	<a href="http://medicprix.sante.gouv.fr/welcome.do">http://medicprix.sante.gouv.fr/welcome.do</a>
France	Ameli l'Assurance Maladie (Reimbursement percentages)	<a href="http://www.ameli.fr/assures/soins-et-remboursements/combien-serez-vous-rembourse/medicaments-et-vaccins/remboursement-des-medicaments-et-tiers-payant/quels-remboursements-pour-vos-medicaments.php">http://www.ameli.fr/assures/soins-et-remboursements/combien-serez-vous-rembourse/medicaments-et-vaccins/remboursement-des-medicaments-et-tiers-payant/quels-remboursements-pour-vos-medicaments.php</a>
Germany	German DIMDI reimbursement prices	<a href="http://www.dimdi.de/static/en/amg/fbag/index.htm">http://www.dimdi.de/static/en/amg/fbag/index.htm</a>
Hungary	The Common European Drug Database	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
India	National Pharmaceutical Pricing Authority	<a href="http://www.nppaindia.nic.in/index1.html">http://www.nppaindia.nic.in/index1.html</a>
India	Tamil Nadu Medical Services Corporation	<a href="http://www.tnmsc.com/">http://www.tnmsc.com/</a>
Iran	Ministry of Health and Medical Education: Food and Drug Department	<a href="http://www.fdo.ir/Drug/Fa/Downloads/ShowSection.aspx?fid=11">http://www.fdo.ir/Drug/Fa/Downloads/ShowSection.aspx?fid=11</a>
Ireland	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Italy	L'Agenzia Italiana del farmaco (AIFA)	<a href="http://farmaco.agenziafarmaco.it/index.php">http://farmaco.agenziafarmaco.it/index.php</a>

COUNTRY	TITLE	WEBSITE
Jordan	Jordan Food and Drug Administration (JFDA)	<a href="http://www.jfda.jo/barcode_java/index.jsp">http://www.jfda.jo/barcode_java/index.jsp</a>
Latvia	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Lebanon	Ministry of Public Health: Drugs Public Price List G	<a href="http://www.moph.gov.lb/Drugs/Pages/Drugs.aspx">http://www.moph.gov.lb/Drugs/Pages/Drugs.aspx</a>
Lithuania	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Morocco	Agence Nationale de L'assurance Maladie	<a href="http://www.assurancemaladie.ma/anam.php?id_espace=6&amp;id_srub=19">http://www.assurancemaladie.ma/anam.php?id_espace=6&amp;id_srub=19</a>
Netherlands	College voor Zorgverzekeringen (CVZ)	<a href="http://www.medicijnkosten.nl/">http://www.medicijnkosten.nl/</a>
New Zealand	The Pharmaceutical Management Agency (PHARMAC)	<a href="http://www.pharmac.govt.nz/healthpros">http://www.pharmac.govt.nz/healthpros</a>
Norway	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Norway	Statens legemiddelverket	<a href="http://www.legemiddelverket.no/templates/InterPage_38824.aspx?filterBy=CopyToMedecs">http://www.legemiddelverket.no/templates/InterPage_38824.aspx?filterBy=CopyToMedecs</a>
Oman	Ministry of Health	<a href="http://www.moh.gov.om/nv_menu.php?fNm=pharma/internetprices.htm&amp;SP=1">http://www.moh.gov.om/nv_menu.php?fNm=pharma/internetprices.htm&amp;SP=1</a>
Poland	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Portugal	National Authority of Medicines and Health products) INFARMED	<a href="http://www.infarmed.pt/infomed/inicio.php">http://www.infarmed.pt/infomed/inicio.php</a>
Portugal	Guia dos Medicamentos Genéricos e Precos de Referência	<a href="http://www.infarmed.pt/genericos/menu.html">http://www.infarmed.pt/genericos/menu.html</a>
Slovakia	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
Slovenia	The Common European Drug Database (CEDD)	<a href="http://cedd.oep.hu/">http://cedd.oep.hu/</a>
South Africa	Department of Health	<a href="http://www.doh.gov.za/docs/misc/asepi-f.html">http://www.doh.gov.za/docs/misc/asepi-f.html</a>
South Africa	Department of Health - Database of Medicine Prices	<a href="http://www.doh.gov.za/department/medic_prices-f.html">http://www.doh.gov.za/department/medic_prices-f.html</a>
South Africa	Treatment Action Campaign: Public sector ARV tender prices	<a href="http://www.tac.org.za/community/node/2027">http://www.tac.org.za/community/node/2027</a>
Spain	Agencia Espana de Medicamentos y Productos Sanitarios (AEMPS)	<a href="https://sinaem4.agemed.es/consaem/fichasTecnicas.do">https://sinaem4.agemed.es/consaem/fichasTecnicas.do</a>
Spain	Informacion de Medicamentos y Principios Activos	<a href="http://www.vademecum.es/">http://www.vademecum.es/</a>
Sudan	Federal Pharmacy and Poisons Board - Sudan Index	<a href="http://www.nmpb.gov.sd/drugsearch.php">http://www.nmpb.gov.sd/drugsearch.php</a>
Sweden	The Dental and Pharmaceutical Benefits Agency (TLV)	<a href="http://www.tlv.se/in-english/">http://www.tlv.se/in-english/</a>
Tunisia	La Pharmacie Centrale de Tunisie	<a href="http://www.phct.com.tn/fr/produits.php#">http://www.phct.com.tn/fr/produits.php#</a>
United Kingdom	Drug Tariff for Scotland	<a href="http://www.isdscotland.org/isd/2245.html">http://www.isdscotland.org/isd/2245.html</a>
United Kingdom	NHS Generic Pharmaceuticals electronic Market Information Tool (eMIT)	<a href="http://www.pasa.nhs.uk/PASAWeb/Productsandservices/Pharmaceuticals/">http://www.pasa.nhs.uk/PASAWeb/Productsandservices/Pharmaceuticals/</a>

COUNTRY	TITLE	WEBSITE
United Kingdom	British National Formulary	<a href="http://bnf.org/bnf/index.htm">http://bnf.org/bnf/index.htm</a>
United Kingdom	National Health Service Drug Tariff for England and Wales	<a href="http://www.ppa.org.uk/ppa/edt_intro.htm">http://www.ppa.org.uk/ppa/edt_intro.htm</a>
United States	Department of Veterans Affairs	<a href="http://www.pbm.va.gov/ContractsAndAgreements.aspx">http://www.pbm.va.gov/ContractsAndAgreements.aspx</a>
United States	MEDICAID	<a href="http://www.cms.hhs.gov/Reimbursement/">http://www.cms.hhs.gov/Reimbursement/</a>
United States	Kentucky MEDICAID Services	<a href="http://chfs.ky.gov/dms/maximum.htm">http://chfs.ky.gov/dms/maximum.htm</a>
United States	Centers for Disease Control (CDC) - Vaccine Price List	<a href="http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm">http://www.cdc.gov/vaccines/programs/vfc/cdc-vac-price-list.htm</a>