Too Costly & Too Scarce

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Chapter 1

Introduction

1.1 GENERAL INTRODUCTION

"I developed high blood pressure because of stress...But I did not have money to buy the medicine. I asked my daughter and she gave me 100 shillings. That didn't help me because the medicine cost 500 shillings. With the 100 shillings I could only buy some of the medicine. It didn't help much... I was told that chewing garlic would help. But my ulcers worsened. I was then asked to pay 300 shillings to get tablets for ulcers but I did not have the money. Now I had ulcers and high blood pressure. So whatever little money I was lucky to lay my hands on could only go into treating one of these complications, letting the other worsen. The people I have approached for help tell me they too do not have money....At the nearby government health centre, I pay 20 shillings but rarely do I get all the medicine I need. They tell me to go buy the rest yet I do not have money. I take garlic but it worsens my ulcers. I have no choice but to use it to reduce my blood pressure and endure the pain afterwards."

Interview with Mbithe Munyao, Kenya, 2010

High medicine prices know no bounds – they affect all countries, all diseases, and affect all people (both directly and indirectly). But the greatest price is paid by the poor who are forced to pay for medicines out-of-pocket. Coupled with this, the availability of medicines in outlets can be low, as illustrated by Mbithe Munyao's story (1).

This thesis aims to firstly shed light on the price governments and people pay for medicines in low- and middle-income countries (LMICs), the affordability of medicines for people on low incomes, and the availability of medicines in outlets. The second aim is to assess the impact of three factors on the price and availability of medicines: inclusion in the national essential medicines list (EML), price transparency and comparing prices paid by other government purchasers, and local medicine production.

Medicine availability and affordability problems and their consequences

In a large number of LMICs, up to 90% of the population purchase medicines out-of-pocket (2,3). Medicines account for a significant proportion of personal or household income. Across 51 LMICs, health care expenditure accounted for 13% to 32% of total four-week household expenditure, and between 41% and 56% of households spent all of their health care expenditure on medicines (4). Even in high-income countries (HICs), affording medicines can be problematic e.g. in Australia a substantial minority (28%) of people experienced a level of financial burden when obtaining medicines (5).

Across eight LMICs, the top two reasons given for adults and children not obtaining health care were not being able to afford medicines (54%), and not being able to find them in outlets (29%) (6). In Kenya and Guinea, lack of funds resulted in 58% and 22%, respectively, of people not buying the medicines they need or buying less than was needed (7).

McIntyre and colleagues (2006) described various strategies used by people in LMICs when faced with high health care costs which, in many cases may trigger devastating and long-term consequences for the family (8). Savings can be used to pay health care costs, although this was shown to be feasible for only a small proportion of households. Many borrow money from family, friends and money-lenders, with some households remaining in debt for a considerable time after the illness. Some households reduce consumption of other goods (often food) and/or sell assets. Selling assets integral to a household's livelihood, such as land or livestock in a rural setting, may trigger impoverishment. Some households take on extra work, or re-allocate work among household members which may have adverse consequences particularly when children are removed from school to take on the work of a sick parent.

Governments are responsible to ensure access to medicines

Low public sector availability and high unaffordable private sector prices are key barriers to accessing medicines in LMICs, which hinders health and hence development (2). In HICs, where most medicines are reimbursed, the buyer has the most power (governments,

insurance companies etc.). In LMICs, where most medicines are paid for out-of-pocket by patients, the seller has the greatest power. Because patients are largely powerless when it comes to accessing medicines, the government is considered the actor who should ensure that essential medicines are available and affordable for all their citizens (9).

The right to the highest attainable standard of health is enshrined in international treaties and legislation in many countries (10). Access to essential medicines, as part of attainment of the right to health, is a crucial element in the progressive fulfillment of the right to health (10). Therefore, regardless of moral and ethical judgments, if the right to health is enshrined in law, the right to essential medicines can be claimed. Thus it becomes the responsibility of governments to ensure their citizens can access the health care they need and crucially, in the context of this thesis, access to medicines. This is particularly challenging as most countries face a demographic transition, with more older people needing medicines. In addition, there has been an epidemiologic transition from acute conditions to chronic conditions (11). In many cases, governments cannot even adequately fund a department that will take responsibility for ensuring access to medicines.

Emergence of access and medicine price issues on the political agenda

At the international level, mobilisation started about 40 years ago with the Alma-Ata Declaration on Health for All in 1978. This provided a comprehensive vision and framework for health services based on primary health care, declaring that "the attainment of the highest possible level of health is a most important world-wide social goal" (12). By including the provision of essential medicines as one of the eight listed components of primary health care, it established the link between the social goal of the highest possible level of health and access to essential medicines (10).

The World Health Organization (WHO) launched the first Model List of Essential Medicines in 1977, setting the scene for essential medicines as an integral part of the Health for All strategy (13). The Model List was a compilation of essential medicines that could be adapted to national needs and serve as a guideline for establishing national lists. Back then, about a dozen countries had what would now be considered an EML or an essential medicines programme[1].

In 1985, the Nairobi Conference of Experts on the Rational Use of Drugs was held. It was considered a milestone in the process of developing policies to improve the use of essential medicines (14). Following the conference, various policy guidelines were developed on the procurement, supply, prescribing and dispensing of medicines, and the

[1] According to WHO, 156 countries now have a national essential medicines list.

regulation of pharmaceutical promotion. This included the first edition of the Guidelines for Developing National Drug Policies in 1988 (15).

As a result of the Alma-Ata declaration, the Nairobi Conference and the publication of the Model List of Essential Medicines, WHO established the Action Program for Essential Drugs which supported countries in developing essential medicines programmes. These programmes usually included establishing national EMLs, and improved public sector procurement and distribution.

Following requests from member states for advice on measures to control medicine expenditure, WHO's Regional Office for Europe published the first edition of *Drugs and Money* in 1983 which gave an overview of the effectiveness of various medicine cost-containment schemes (16). It was not until the seventh and final edition, published in 2003, that consideration was given to the use of cost-containment schemes in developing countries and countries in transition. But, as with the earlier editions, in-depth guidance was lacking as little was known about pricing practices, and policy options and their impact, in LMICs (17).

In 1986, Management Sciences for Health (MSH) published the first International Drug Price Indicator Guide (Guide). The Guide, which is publicly available and published annually, lists selling and buying prices from a number of pharmaceutical suppliers to procurement agencies/governments in LMICs and international development organizations (18). The prices are real, but are not patient prices. Rather, they are large volume international procurement prices. However, they serve as an invaluable stable multinational reference price for multi-source products. Over time, the Guide has expanded with more medicines and more prices listed.

The 1988 WHO World Drug Situation Report did not contain any information on prices, and only a few vague references to the use of generics (19). Government control over medicine prices was considered to be largely lost in the 1990s (20). The impact of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) on access to new medicines was increasingly being discussed in the second half of the 1990s (21,22) but information on the price, availability and affordability of existing, commonly-used medicines in pharmacies and health facilities in LMICs was poor to virtually non-existent up until the 2000s (when the work in this thesis started). Pricing policies were implemented mostly in HICs with robust reimbursement and/or health systems (16,23). Some LMICs regulated or set prices (eg. Pakistan, India, Morocco, Sri Lanka and Syria (20,24-27) but their impact was rarely, if ever, evaluated.

Up until the early 2000s, governments in LMICs, wanting to contain expenditure on medicines and reduce financial hardship for patients when buying medicines, had little understanding of prices and affordability. They did not know how to reliably assess whether their procurement prices were competitive or not, nor how to assess what patients actually pay, and whether or not treatments were affordable in various sectors and regions of their country. Only a few small-scale price studies in LMICs had been undertaken at that time, many of which lacked methodological rigor (28,29). Governments also had limited knowledge of factors that influence prices and availability, policy options available to them, and the pros and cons of each in various settings. In short, they faced two issues: how to reliably collect the evidence and, once collected, what to do to improve availability and/or lower prices.

WHO/HAI Project on Medicine Prices and Availability

In late 1990s, several civil society organisations, including Health Action International (HAI) started drawing attention to the high prices of medicines. High prices in LMICs were discussed with WHO at the WHO/Public Interest Non-governmental Organisations (NGO) Roundtables held in the late 1990s. The absence of a standard methodology was seen as a stumbling block in reliable price measurement. Therefore, in 2001, the WHO/HAI Project on Medicine Prices and Availability was established to: (1) develop a reliable methodology for collecting and analysing medicine price, availability, affordability and price component data; (2) publish survey data on a publicly accessible website to improve price transparency; and (3) advocate for appropriate national policies and monitor their impact.

In 2001 and 2002, the World Health Assembly (WHA) supported the project via two resolutions (31,32). At the WHA in 2003, WHO and HAI, with the support of a group of international experts, published their methodology to measure medicine prices, availability, affordability and price components based on nine pilot studies (33). To improve price transparency and allow international comparisons, a publicly-accessible database (34) of survey results was established on HAI's website (http://haiweb.org/what-we-do/price-availability-affordability/price-availability-data/). The second edition of the methodology manual was published in 2008 (35). To date, over 100 national or subnational surveys have been conducted, in all regions of the world, predominantly by Ministry of Health personnel, academics, and NGOs (36-49). To assist national policy-makers on the design and implementation of various pricing policy approaches, WHO and HAI published

reviews and policy briefs on various policies and interventions to improve medicine availability and make medicines more affordable, with a focus on LMICs (50-55).

Little attention on commonly used medicines for NCDs

During the period when the WHO/HAI methodology was being developed and many surveys undertaken, considerable progress in ensuring the availability of treatment for key infectious diseases (HIV/AIDS, malaria and tuberculosis) occurred. The Global Fund to Fight AIDS, Tuberculosis and Malaria and UNITAID were founded, and major infectious disease programmes were established by WHO and other organisations such that medicines for these diseases became more widely available and were generally free-of-charge. However, whilst infectious disease programmes proved successful, the importance and significance of non-communicable diseases (NCDs) remained neglected.

NCDs are now the world's biggest killers. Over 36 million people die annually from NCDs (63% of global deaths) and of these, 80% occur in LMICs (56). Since 2006, many organisations and groups, from the United Nations (UN) General Assembly and WHO to governments and NGOs, have turned their attention to improving access to medicines to treat NCDs. When developing WHO's Global Action Plan for the Prevention and Control of NCDs, many groups and individuals advocated for the inclusion of a target on both the availability and affordability of medicines. Hence the target of 80% availability of affordable NCD medicines, including generics, in the public and private sectors by 2025 was adopted in the Global Action Plan (57). In contrast to the global response to infectious diseases, there has been very limited additional support for NCDs and what interest had been generated is now being overtaken by concern about anti-microbial resistance. The UN, governments, civil society and the media also appear more focused on improving access to the extremely high-priced new medicines to treat cancer, Hepatitis C and other conditions, rather than existing, effective, commonly-used, lower-priced essential but still unaffordable medicines (58,59).

This thesis describes the work undertaken since 2001 to develop the WHO/HAI survey tools, to measure medicine prices, availability, affordability and price components, to identify policy options, and to assess the effect of several factors on availability and prices. It is part of an international effort to draw attention to the issues, assist governments to develop evidence-based policies to make medicines more available and affordable, and inform civil society and others when advocating for change.

1.2 THEORETICAL FRAMEWORK

The previous section elucidated the background to the thesis and the aims of the research. This section of the introduction describes the theoretical framework, the underlying concepts, and the hypotheses formulated based on these concepts.

Definitions

For the sake of clarity, the following definitions are given:

- *Price*: The price of a medicine is taken as the price paid by a patient/consumer when buying a medicine in an outlet (patient price), or the price paid by government agencies when procuring a medicine (government procurement price or public sector procurement price). In the WHO/HAI methodology, prices are expressed in local currency and also as a ratio to an international reference price (35).
- *Availability*: The availability of a medicine is a one-point-in-time measurement on whether or not the medicine is in stock in an outlet (35).
- *Affordability*: The affordability of a treatment is based on personal income and the price of the treatment. WHO/HAI expresses affordability as the number of days' wages the lowest-paid unskilled government worker has to pay to purchase a course of treatment for an acute condition or a 30 day supply for an NCD medicine, based on standard regimens (35).
- *Medicine price components*: These are all the add-on charges in the pharmaceutical supply chain from the manufacturer's selling price to the patient price i.e. mark-ups, taxes, tariffs, clearance costs, etc. (35).

Access to medicines frameworks

Contrary to the situation found in the 1980s and 90s, various access to medicines frameworks and determinants are now in existence. In 2000, WHO and MSH published a framework comprising four determinants – medicine availability, affordability, acceptability and accessibility – with quality of products and services as a cross-cutting determinant (60). In 2004, WHO published a framework, also with four determinants – affordable prices, sustainable financing, reliable health, and supply systems and rational use – plus product quality assurance as a cross-cutting determinant (61). In 2010, Frost and Reich proposed a framework with three determinants – availability, affordability and adoption – with organisational relationships at national and international levels as a cross-cutting determinant (62). All three frameworks include medicine availability and

affordability, underlining the significance of these determinants as barriers to accessing medicines. But, as pointed out by Bigdeli and colleagues (2013), barriers to accessing medicines are complex and occur at multiple levels of health systems (63).

Bigdeli and colleagues (2013) considered that these former frameworks did not address the complexity of access to medicines issues and proposed a conceptual framework that took a health system approach – see Figure 1 (63). The complexity of influences, and their interconnectivity, may account for access to medicines remaining poor despite the plethora of policies and interventions aimed at improving the situation.

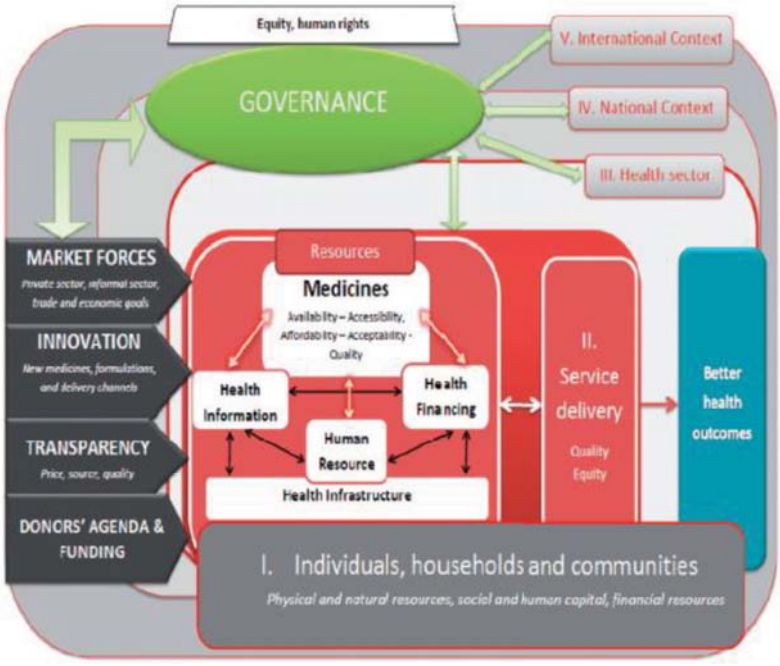

Figure 1: Access to medicines from a health system perspective: a conceptual framework (Bigdeli et al., 2016)

Factors influencing medicine prices, availability and affordability

Using the framework of Bigdeli and colleagues, factors in various contexts that can influence the price, availability and affordability of medicines can be identified. They include:

- *Level 1:* individuals, households and communities
  Key factors include the income of the individual or household, the medicine(s) needed by the individual or household, the sector where medicines are obtained, the ability to shop around, knowledge and perceptions on the quality of products (including low-priced generics and locally produced products), and the impact of any direct-to-consumer advertising of medicines.
- *Level 2:* health service delivery
  These include an absence of reliable procurement sources, irregular supplies, location of outlets, what products are stocked, the interaction between the pharmacy and patient when medicines are dispensed, perverse prescribing and dispensing incentives.
- *Level 3:* health and pharmaceutical sectors
  - In the pharmaceutical sector these include government medicine procurement processes (use of essential medicines lists and formularies to select medicines to be procured, forecasting need, the procurement process, paying suppliers on time), price control strategies (policies promoting the use of generics, mark-up regulations and others), the pharmaceutical budget and medicine financing, and outpatient medicines benefits in insurance schemes.
  - In the health sector these include health policy and legislation, the health budget, national health insurance schemes and their coverage, and morbidity and mortality profiles.
- *Level 4:* national context
  These include trade and procurement factors (such as intellectual property law, competition law, policies on taxation and tariffs, industrial policy, and government procurement policy), the national budget, and human rights laws.
- *Level 5:* international context
  These include bi-lateral or multi-lateral trade agreements, intellectual property agreements, use of patent pools, multi-country pooled procurement, global health partnerships that finance and/or procure medicines, manufacturing and marketing strategies of companies, differential pricing initiatives of companies, exchange rate fluctuations and donor agendas.

The complexity and interplay between factors is daunting, especially when dubious governance, opacity and politics are factored into the equation. But at the core of the access issue are the enduring problems of medicine prices, availability, and affordability. It is here that this thesis will focus – whether the medicine is on the shelf when a patient

needs it, how much it costs, and whether it is affordable. The pharmaceutical market is complex, but prices and availability are measurable. However, data on prices, availability, and affordability are fragmented and scarce.

Evidence is the first step to improving access

Evidence on the price, availability, and affordability of medicines is a key step in describing and understanding barriers to access. It is the inevitable starting point for any intervention that attempts to have an impact on the lives of those denied treatment. Of course, evidence alone can never improve access. Greater clarity on *why* prices and availability are high or low, or medicines are affordable or are not affordable, is needed to inform the policy development process and, ultimately, improve access. Thus, a clear understanding on what factors influence prices, availability and affordability and their relationship with each other is vital – in short, a holistic health systems perspective is needed. This is frequently ignored in the effort to create a quick-fix to access issues; in many attempts the pharmaceutical sector itself is not considered, neither are factors related to the national and global context. As a consequence, access to medicines is addressed through fragmented, vertical approaches usually focusing on supply only.

At the core of access to medicines problems is the paucity of medicine price, availability, and affordability data. Is a course of treatment affordable to a patient on a low income in a low-income country? Are medicines available in pharmacies? Are governments buying medicines at competitive prices? What premium are people paying to buy originator brands?

The quality, acceptability, and accessibility of medicines are important, as pointed out by Bigdeli. However, for the sake of pragmatism, they are not addressed in this thesis.

Hypotheses

Based on the above analysis of the literature and what is not known, there is a need to better understand the factors that influence access in terms of public sector procurement and patient prices, availability, and affordability. Therefore the hypotheses of this thesis are:

H1 A robust methodology allows for the collection, analysis and reporting of medicine prices, availability, affordability and price components as a basis for developing policies and responses to improve access to medicines

H1.1 Medicine availability is suboptimal and affordability is poor in LMICs, and availability and affordability cannot be considered in isolation

H1.2 Barriers at various levels impact medicine availability, prices and affordability

H1.3 Governments in LMICs are procuring medicines at prices far above international reference prices

H2 Identified policy interventions will influence medicine prices and availability

H2.1 Essential medicines lists have a positive effect on availability

H2.2 Analysing procurement prices can lead to positive outcomes for the procurement process

H2.3 Local production results in lower prices and improved availability

1.3 RESEARCH DESIGN

To determine whether the hypotheses are supported or not, the thesis needs to answer the following questions.

1.3.1 Research questions

The main research question of this thesis has been formulated as follows:

What is the price, availability, affordability, and price components of commonly used medicines in LMICs and what are some of the factors influencing prices and availability?

One of the hypotheses in this thesis is that to improve access, medicines must be both available in outlets when needed and affordable when patients have to purchase them. When developing policies to improve medicine availability and affordability, national policy-makers firstly need clarity on what problems need to be addressed. This requires evidence; what is the availability of medicines in the various sectors in a country where people obtain medicines; what are the prices and affordability of medicines in these sectors; does availability and affordability differ between originator brands and generics and in different regions of a country; is the government paying too much for medicines; what mark-ups and taxes are being applied to medicines, what is the manufacturer's selling price, etc.? When the problems are known, the next step is to identify the key factors that influence the problem. As discussed above, multiple and often interlinked factors can influence availability, prices, and affordability, and they can differ across

countries. Identifying the key factors causing the problems is a vital step in the policy development process.
To answer the main research question, two sub-questions have been formulated:

(1) In LMICs, what is the availability, price, affordability, and price components of medicines used to treat communicable diseases and NCDs?

This questions the actual availability, price, affordability, and price components of medicines in LMICs. Firstly, an overarching perspective is sought, including medicines to treat both communicable and NCDs, with data about their availability, price and affordability assessed individually. Secondly, as a case study, the availability, price and affordability of insulin is investigated, a medicine essential for the survival of people with type 1 diabetes and increasingly being used by people with type 2 diabetes. Again, these indicators of access are assessed individually. Thirdly, building on the foregoing, the question relates to the combined availability and affordability of medicines to treat four common NCDs: cardiovascular diseases, diabetes, chronic obstructive pulmonary diseases and central nervous system conditions.

(2) In LMICs, what is the influence of the following factors on availability and/or prices:
- *(a) Inclusion of medicines in national EMLs?*
- *(b) Public sector procurement and price transparency?*
- *(c) Local medicine production?*

These questions ask about the influence of three specific factors on medicine availability and/or prices. The first question focuses solely on availability, and asks whether inclusion in a national EML results in greater availability in outlets. The second question focuses on public sector procurement of medicines, and the influence of price transparency and comparing prices paid by other purchasers, to identify potential savings. The final question asks if local medicine production influences the availability and prices of medicines in outlets in the manufacturing country.

1.3.2 Research approach

This thesis used a mixed-methods approach to answer the research questions i.e. analyses using primary data and secondary analyses. Based on the WHO/HAI methodology, country specific data was used to assess medicine availability, prices and affordability in LMICs. These results were complemented by secondary analyses of specific survey data, as well as reviews to highlight specific challenges. For example, the use of target disease

areas (NCDs: Chapter 4), specific medicines (insulin: Chapter 3), policy responses (local production: Chapter 7) as well as contexts (UNRWA: Chapter 6) to highlight the diversity of barriers to access to medicines. This approach also enabled an assessment of WHO targets on medicine availability and affordability, the development of specific policy recommendations, and contributes to the overall understanding of the complexity of the factors that impact the availability and affordability of medicines.

The thesis consists of six studies:

Study 1. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis

This is a secondary analysis to consolidate what is known about medicine prices, availability, and affordability from 45 national and subnational surveys conducted in 36 LMICs using the WHO/HAI methodology. The WHO/HAI methodology is described in *Box 1.* In this study, data were analysed for 15 commonly used medicines to treat key acute communicable diseases and chronic NCDs. Government procurement prices were analysed, and patient prices, affordability, and availability in the public and private sectors of the countries. Price components were also measured in a few of the countries. Various policy options to address issues of high prices and low availability are discussed. This study provides a comprehensive and reliable overview of the current situation as it includes all three key indicators of access (availability, price, and affordability), medicines used to treat both communicable and NCDs, data from a large number of LMICs, and surveys that were undertaken using a standardised and robust approach.

Study 2. Constraints and challenges in access to insulin: a global perspective

Although insulin was first used to treat diabetes nearly a century ago, access can be poor in both developing and developed countries. This translates into a life expectancy of one year for a child with type 1 diabetes in sub-Saharan Africa (64). Despite the absolute necessity for access to this medicine and the UN political commitment to address NCDs and ensure universal access to medicines for diabetes, up until 2015 it attracted little global attention. In this literature review, the range and complexity of factors that contribute to poor access to insulin are highlighted, including availability, patient prices, and affordability, and a call for action is made to improve the situation. The study was undertaken as part of the 'Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) Study' which was launched in early 2015. The ACCISS Study is a collaboration between HAI,

Geneva University Hospitals and the University of Geneva, and Boston University School of Public Health (65).

Study 3. Baseline assessment of WHO's target for both availability and affordability of medicines to treat non-communicable diseases

WHO has set a voluntary target of 80% availability of affordable medicines, including generics, to treat major NCDs in the public and private sectors of countries by 2025 (57). This study is a secondary analysis of availability and affordability data from 30 surveys, conducted in LMICs using the WHO/HAI methodology to establish a baseline for the target for four NCDs: diabetes, cardiovascular disease, chronic obstructive airways diseases and central nervous system disorders. Whilst Study 1 assessed medicine availability and affordability individually, this study took the additional and innovative step of analysing availability and affordability in combination. This is a more robust indicator of access as medicines need to be both available in facilities when needed, and either free-of-charge or affordable when purchased.

Study 4. Essential medicines are more available than other medicines around the globe

WHO promotes the development of national EMLs in order to improve the availability and use of medicines considered essential within health care systems. According to WHO, EMLs exist in 156 countries; of these over 90% use the EML as a basis for public procurement of medicines. However, having an EML does not guarantee the availability of essential medicines in outlets. In this study, the availability of medicines included in the national EML was compared with those which are not on the national EML in 23 countries, using availability data from the WHO/HAI database. The aim was to ascertain if inclusion of medicines in national EMLs improved their availability in public and private sector outlets.

Study 5. Comparative assessment of medicine procurement prices in the United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA)

UNRWA, the primary healthcare provider for 4.9 million Palestinian refugees, spent USD18.3 million on essential medicines dispensed free-of-charge through a total of 137 primary healthcare clinics and one hospital in their five areas of operation, namely, Gaza, Jordan, Lebanon, Syria, and the West Bank (66). Faced with budget constraints and an increasing demand for medicines to treat NCDs, in this study UNRWA's medicine procurement prices were assessed to see if savings could be possible. UNRWA's prices and quantities procured were compared with those from a neighbouring and host country

(Jordan), a regional procurement organisation (Gulf Co-operation Council, GCC), a non-profit international supplier (the IDA Foundation), and MSH prices. The aim of comparing prices across a range of comparators was to answer the question "would savings result if UNRWA was to procure differently", and to ascertain whether price transparency and undertaking price comparisons is empowering when procuring medicines.

Study 6. Prices and availability of locally produced and imported medicines in Ethiopia and Tanzania

Increasingly, governments in LMICs are supporting local production of medicines, expecting it to improve access to medicines as well as provide industrial and economic benefits. However, the literature is inconclusive on whether or not local production improves access (67). When looking at patient prices, three studies (68-70) showed locally produced products were generally lower priced than imported products, and one study found the opposite (71).

There is no standard methodology to compare the price and availability of locally produced and imported medicines, which may account for the small number of studies on these two indicators of access. So, in this study, the WHO/HAI methodology was adapted to measure and compare the availability and prices (government procurement prices and patient prices) of locally produced and imported medicines. The new tool was piloted in Ethiopia and Tanzania. In addition to describing the new tool and the findings from the two pilot surveys, recommendations to governments supporting local medicine production are given to help ensure patients benefit from this policy through improved availability and lower prices.

An overview of the thesis sub-questions, studies, research methods, and chapters is provided in Table 1.

Table 1. Overview of thesis sub-questions, studies, methodologies and location of the studies in the thesis

Study	Thesis sub-questions						Chapter
	What is the availability, price, and/or affordability, individually or in combination, of:			What is the influence of the following factors on availability, price, and/or affordability:			
	(a) Medicines used to treat CD and NCDs?	(b) Insulin?	(c) Medicines used to treat four major NCDs?	(a) Inclusion of medicines in national EMLs?	(b) Public sector procurement and price transparency?	(c) Local medicine production?	
1	Secondary analysis of datasets						2
2		Systematic literature review and analysis					3
3			Secondary analysis of combination data on availability and affordability				4
4				Comparative analysis			5
5					Comparative analysis		6
6						Comparative analysis	7

Box 1. **WHO/HAI methodology to measure medicine prices, availability, affordability, and price components**

The WHO/HAI methodology (35) is a facility-based survey of the availability and price of 50 medicines to treat communicable diseases and NCDs, in a minimum of six geographic areas. Data are collected in a sample of medicine outlets in the public sector, private sector, and up to two other sectors (e.g. mission hospitals). Data are also collected on government procurement prices and price components in the pharmaceutical supply chain (mark-ups, taxes etc.).

Data are collected from five outlets per sector per area. The selection of outlets uses a multistage clustered approach. Survey areas include the capital plus five areas randomly selected from those that can be reached within one day's travel from the capital. In each area, the main public hospital and four randomly-selected primary health care outlets, reachable within four hours' travel from the hospital, make up the public sector sample. The private sector (licensed pharmacies and licensed drug outlets) and other sector samples are identified by selecting one outlet in each sector that is geographically closest to each public outlet.

Survey medicines include a global core list of medicines (14), all strength- and dosage-form specific, commonly used to treat a range of conditions that cause substantial morbidity and mortality (e.g. hypertension, diabetes, respiratory tract infection). At least 36 supplementary medicines of local importance are also surveyed. Prior to 2016, the following medicines were surveyed: 14 global list, 16 regional list, and 20 supplementary. For each medicine, data are collected for the originator brand, and the lowest-priced generic equivalent found in each outlet.

Trained data collectors visit medicine outlets and record availability and price using a standardised form. Data are entered into a preprogrammed Excel spreadsheet that accompanies the manual. Several validation and data checking steps ensure data quality (see Section 1.3.3).

Box 1. **WHO/HAI methodology to measure medicine prices, availability, affordability, and price components** *(Continued)*

Data are analysed by sector for individual medicines and for the basket of medicines. Availability is reported as the percentage of outlets where the medicine was in stock on the day of data collection. Availability takes into account the level at which outlets in the public sector are permitted to stock each medicine. Prices are expressed as medians in local currency, and as a ratio to international reference prices. The international reference prices used are median supplier prices (or buyer prices where there are no supplier prices) listed in MSH's Guide. A minimum of four patient prices per medicine per sector is needed for inclusion in the analysis. Affordability is based on the median price in local currency for a standard treatment regimen, and expressed as the number of days' wages needed by the lowest-paid unskilled government worker to purchase 30 days' supply of the medicine to treat NCDs, and seven days' supply for medicines to treat communicable diseases. WHO considers patient prices high when they are over four times the international reference price (72). WHO and HAI consider treatments as unaffordable if the lowest-paid unskilled government worker has to pay more than one day's wage for a course of treatment for an acute condition, or a 30 day supply for a chronic condition, based on standard treatment regimens (37).

The author's role in the studies

The author of this thesis has coordinated the WHO/HAI Project on Medicine Prices and Availability since its inception in 2001. This has involved co-designing and co-drafting the research methodology in collaboration with WHO and other experts; training national research investigators and providing technical support including ensuring data quality; results analysis; recommendation of evidence-based policy interventions, and working with experts on reviews of various pricing policies. The author also designed the WHO/HAI online database of survey findings, and adds new data on an ongoing basis. This open-source multi-national database of public sector procurement prices, patient prices, availability, affordability, and price components is both unique and valuable, with data regularly cited.

It is the WHO/HAI database that provided the data for the secondary analyses of prices, availability, and affordability in Chapters 2, 4, and 5. The author led the study in Chapter 4, including designing and conducting the analysis, and drafting the article. The author

supported the lead author in the studies in Chapters 2 and 5. For the study in Chapter 2, this involved co-analysing the data, considering the policy recommendations, and reviewing the article. For the study in Chapter 5, the author assisted in the design of the study, reviewed the analyses, and provided extensive comments on the article.

The author also led the study that informs Chapter 6, that is, the review of UNRWA procurement prices. This included designing the study, co-collecting the data at UNRWA headquarters in Jordan, analysing the findings and formulating the recommendations (with the second author), and drafting a report and the article.

The author also led the study that informs Chapter 7 which compares prices of locally produced and imported medicines. This included adapting the WHO/HAI method for this type of study, leading the training of the national research investigators, ensuring data quality, data analysis and formulating the recommendations (with the co-authors), and drafting two national reports and the article.

The analysis described in Chapter 3 was undertaken as part of the ACCISS Study, a first of its kind investigation on improving access to insulin. The author is one of the three principal investigators, and coordinates the study.

1.3.3 Research validity

The WHO/HAI survey methodology's core medicine list and outlet sample approach were validated in a medicine price survey conducted in Peru in 2005 (73). The results showed that including more remote outlets resulted in similar findings to outlets selected using the standardized methodology, and the availability of therapeutic alternatives were generally similar to those of the WHO/HAI core medicines.

Prior to conducting a WHO/HAI survey, investigators are encouraged to conduct a training workshop for survey personnel, and pilot data collection and entry. Guidance is given in the manual on how to conduct this workshop.

Several validation and data checking steps during and after collection ensure data quality. These include:

- data collectors working in pairs so they can each check the products and prices;
- checking data collection form for completeness, legibility, and consistency by area supervisors on the day of data collection;
- validating data collection by the area supervisor repeating the survey in 10% of outlets on the same day of data collection;
- entering the data into a preprogrammed Excel spreadsheet by two people using a double entry technique; and

- cross-checking results by visual inspection and the inbuilt data validation programme highlighting outliers that need verification

As previously stated, the author of this thesis reviews all survey data before it is added to the database. Any data queries are forwarded to the national investigator for checking.

Availability, price, and affordability data used in the secondary analyses were extracted from the WHO/HAI database, reanalysed as required, and then checked by two people.

For the study on prices and availability of locally produced and imported medicines, the two national investigators were trained on the use of the revised tool and provided preprogrammed Excel spreadsheets specific for the survey. Data collection validations and checks were undertaken as per the WHO/HAI methodology, with the exception of an inbuilt data validation programme which is not available. The new automated spreadsheets were tested to ensure all calculations were correct.

1.4 OUTLINE OF THE THESIS

Chapter 1 introduces the thesis. This chapter outlines the problem, theoretical concepts, and research design used in this thesis.

Chapter 2 reports on Study 1 which is a secondary analysis of prices, availability, and affordability (and to a lesser extent on price components) from a large number of national surveys conducted across the globe using the WHO/HAI methodology.

Chapter 3 reports on Study 2 which discusses the challenges of access to insulin at the time the ACCISS Study commenced, including insulin prices, availability, and affordability.

Chapter 4 reports on Study 3 which is a baseline assessment of whether or not WHO's target for NCDs were being met for medicines to treat four common NCDs.

Chapter 5 reports on Study 4 which looks at whether medicines on national EMLs are more available in outlets than 'non-essential' medicines.

Chapter 6 reports on Study 5 which compares prices paid by UNRWA to those paid by other international, regional, and national references, and explores options for UNRWA to save money.

Chapter 7 reports on Study 6 which evaluates the impact of local medicine production on prices and availability.

In the final chapter (Chapter 8) the research sub-questions are answered based on the results of the studies in Chapters 2-7. In addition, conclusions are drawn on what governments and others need to do to improve the availability and affordability of medicines in LMICs based on the evidence.